PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Braftovi™ (encorafenib capsules – Array BioPharma)

TAC APPROVAL DATE: 06/18/2019

OVERVIEW
Braftovi, a BRAF inhibitor, is indicated in combination with Mektovi® (binimetinib tablets), for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, as detected by an FDA-approved test. It is a limitation of use that Braftovi is not indicated for wild-type melanoma.

Disease Overview
Mutations in the BRAF gene are common in several types of cancer. The BRAF protein is normally switched on and off in response to signals that control cell growth and development; however, mutations cause the BRAF protein to be continuously active. This over activity may contribute to the growth of cancers by allowing abnormal cells to grow and divide uncontrollably. The V600E mutation is the most common BRAF gene mutation identified in cancers, particularly in melanoma.

Guidelines
FDA-Approved Indications
NCCN guidelines for melanoma (version 2.2019 – March 12, 2019) recommend BRAF + MEK inhibitor combinations (e.g., Zelboraf [vemurafenib tablets] + Cotellic [cobimetinib tablets], Tafinlar [dabrafenib capsules] + Mekinist [trametinib tablets], Braftovi + Mektovi) for first-line (preferred if clinically needed for early response) and subsequent treatment of metastatic or unresectable melanoma with a V600 activating mutation. While combination BRAF/MEK inhibition is preferred, NCCN notes that if contraindicated, monotherapy with a BRAF inhibitor (Tafinlar or Zelboraf) are recommended options, particularly for patients who are not appropriate candidates for checkpoint immunotherapy. Tafinlar + Mekinist is also recommended in guidelines as adjuvant therapy (including for nodal recurrence) in some patients with Stage III disease, including use post-surgery or use after complete lymph node dissection.

Other Uses With Supportive Evidence
NCCN guidelines for colon cancer (version 2.2019 – May 15, 2019) recommend BRAF/MEK inhibitor combinations for BRAF-V600E mutated disease. For primary treatment (following adjuvant chemotherapy) or as subsequent use, Zelboraf + irinotecan + Erbitux (cetuximab IV infusion) or Vectibix (panitumumab IV infusion) is a recommended treatment option. Subsequent use of either Braftovi + Mekti or Tafinlar + Mekinist are also treatment options recommended in combination with Erbitux or Vectibix.

POLICY STATEMENT
Prior authorization is recommended for prescription benefit coverage of Braftovi. All approvals are provided for the duration noted below.

Automation: None.
RECOMMENDED AUTHORIZATION CRITERIA
Coverage of Braftovi is recommended in those who meet the following criteria:

FDA-Approved Indications
1. **Melanoma.** Approve for 3 years if the patient meets BOTH of the following (A and B):
   A) The patient has unresectable, advanced, or metastatic melanoma; AND
   B) The patient has *BRAF V600* mutation-positive disease.

Other Uses with Supportive Evidence
2. **Colon or Rectal Cancer.** Approve for 3 years if the patient meets the following (A, B, and C):
   A) The patient has *BRAF V600E* mutation-positive disease; AND
   B) The patient has previously received a chemotherapy regimen for colon or rectal cancer.
   NOTE: Examples of chemotherapy regimens include a fluoropyrimidine such as 5-fluorouracil (5-FU), capecitabine; oxaliplatin, irinotecan, or an adjunctive chemotherapy regimen such as FOLFOX (5-FU, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin); AND
   C) The agent is prescribed as part of a combination regimen for colon or rectal cancer. NOTE: examples of combination regimens include: Braftovi/Mektovi (binimetinib tablets)/Erbitux (cetuximab IV infusion), Braftovi/Mektovi/Vectibix (panitumumab IV infusion).

CONDITIONS NOT RECOMMENDED FOR APPROVAL
Braftovi has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

HISTORY

<table>
<thead>
<tr>
<th>Type of Revision</th>
<th>Summary of Changes*</th>
<th>TAC Approval Date</th>
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</thead>
<tbody>
<tr>
<td>New Policy</td>
<td>--</td>
<td>06/27/2018</td>
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<tr>
<td>Annual revision</td>
<td><strong>Colon or Rectal Cancer:</strong> Add criteria as supported by NCCN colon cancer guidelines. Criteria approve if the patient has <em>BRAF V600E</em> mutation-positive disease, and if the patient has previously used chemotherapy, and if Braftovi will be used as part of a combination regimen for colon or rectal cancer.</td>
<td>06/18/2019</td>
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*For a further summary of criteria changes, refer to respective TAC minutes available at: [http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx](http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx). TAC – Therapeutic Assessment Committee; DEU – Drug Evaluation Unit; NCCN – National Comprehensive Cancer Network; NA – Not applicable; NSCLC – Non-small cell lung cancer.