What it does and how it is used

- Vemurafenib (Zelboraf™) is a kinase inhibitor indicated for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation as detected by the FDA approved cobas® 4800 BRAF V600 Mutation Test. Some mutations in the BRAF gene including V600E result in constitutively activated BRAF proteins, can cause cell proliferation in the absence of growth factors that would normally be required for proliferation. Vemurafenib inhibits some mutated forms of BRAF serine-threonine kinase, including BRAF V600E.
- Testing for V600E requires a biopsy, an invasive medical procedure involving a tumor sample. This test may help doctors assess the patient’s prognosis and treatment options.
- Vemurafenib is not recommended for use in patients with wild-type BRAF melanoma.
- Melanoma is a form of skin cancer characterized by the uncontrolled growth of pigment-producing cells (melanocytes) located in the skin. Metastatic melanoma is the deadliest form of the disease, and occurs when cancer spreads beyond the surface of the skin to other organs, such as the lymph nodes, brain, or other areas of the body. Melanoma is mostly curable when treated in its early stages. However, in its late stages, melanoma is generally incurable and median survival ranges from 6 to 15 months.
- Vemurafenib demonstrates a significant improvement in overall response rate among patients with metastatic melanoma with BRAF V600E mutation. Among treatment naïve patients, the overall response rate was 48.4% in the vemurafenib arm compared to 5.5% in the dacarbazine arm. There were 2 complete responses and 104 partial responses in the vemurafenib arm and 12 partial responses in the dacarbazine arm. Among patients who received prior systemic therapy, there was a 52% response rate with 3 complete responses and 66 partial responses. Vemurafenib was not studied in patients with wild-type BRAF melanoma.
- In the clinical trial, 20 patients did not have the BRAF V600E mutation, but were BRAF V600K mutation positive. The patients with the BRAF V600K mutation had a response to vemurafenib, indicating that melanomas with this variant are also sensitive to vemurafenib.
- Vemurafenib is not indicated for the treatment of stage I or stage II non-metastatic melanoma. The National Comprehensive Cancer Network (NCCN) guidelines recommend a variety of treatment options for stage I and stage II melanoma including excision, radiation therapy, local ablation, and imiquimod therapy.
- The recommended dosage regimen for vemurafenib is four 240 mg tablets twice a day. The first dose should be taken in the morning and the second dose should be taken in the evening approximately 12 hours later. It is recommended that patients are treated with vemurafenib until disease progression or unacceptable toxicity occurs.
- Vemurafenib is currently being considered for the treatment of other cancers that are driven by BRAF mutations.

Rationale for coverage authorization
To reduce exposure to cost associated with the use of vemurafenib for conditions for which the effectiveness is not known.

What it costs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Usual Dose</th>
<th>AWP/tablet</th>
<th>AWP/month</th>
<th>AWP/year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zelboraf 240 mg</td>
<td>1,920 mg/day</td>
<td>$47.00</td>
<td>$11,280.00</td>
<td>$135,360.00</td>
</tr>
</tbody>
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Benefit design

- Coverage for Zelboraf™ is determined through prior authorization for every claim.
  AND
- Coverage is provided for a quantity sufficient for treatment of metastatic melanoma.

Coverage authorization criteria

Coverage for vemurafenib is provided in accord with the following criteria:

1. For the treatment of unresectable or metastatic melanoma.
   AND
2. For use in patients with BRAF V600E or BRAF V600K mutation as detected by an FDA-approved test OR CLIA lab-approved reliable assay.
   AND
3. Coverage is not provided in combination with ipilimumab.

Coverage duration:
Coverage duration is provided for 6 months. Coverage may be renewed.

Quantity duration limit:
Coverage is provided for up to 8 tablets per day (960 mg twice daily).
Additional quantities are not provided.

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<th>References</th>
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