# vemurafenib (Zelboraf®)

EOCCO POLICY

## Policy Type: PA/SP/NF  Pharmacy Coverage Policy: EOCCO070

### Description

Vemurafenib (Zelboraf) is an orally administered BRAF kinase inhibitor used for the treatment of unresectable or metastatic melanoma, or Erdheim-Chester Disease in patients with a BRAFV600E mutation.

### Length of Authorization

- Initial: Three months
- Renewal: 12 months

### Quantity limits

| Product Name | Dosage Form | Indication | Quantity Limit | DDID |
|---|---|---|---|---|
| vemurafenib (Zelboraf) | 240 mg tablets | Unresectable or mestastatic melanoma; Erdheim-Chester Disease | 240 tablets/30 days | 168496 |

### Initial Evaluation

I. Vemurafenib (Zelboraf) may be considered medically necessary when the following criteria below are met:
   A. Prescribed by or in consultation with an oncologist; **AND**
   B. A diagnosis of one of the following:
      1. **Unresectable or metastatic melanoma**; **AND**
         i. Documented BRAF V600E mutation by an FDA-approved test; **AND**
         ii. To be used in combination with cobimetinib (Cotellic); **OR**
      2. **Erdheim-Chester Disease**; **AND**
         i. Documented BRAF V600E mutation by an FDA-approved test

II. Vemurafenib (Zelboraf) is considered <u>investigational</u> when used for all other conditions, including but <u>not limited to</u>:
   A. Thyroid cancer (e.g. anaplastic thyroid carcinoma, advanced papillary thyroid cancers with BRAF v600 mutation)
   B. Non-small cell lung cancer (NSCLC) with BRAF V600E mutation
   C. Hairy cell leukemia

## Renewal Evaluation

I. Member has previously received treatment with vemurafenib (Zelboraf); **AND**
II. Continues to meet criteria identified in section I of the Initial Evaluation; **AND**
III. Absence of disease progression; **AND**
IV. Absence of unacceptable toxicity from the medication

## Supporting Evidence

I. FDA-approved companion diagnostic for BRAF V600E mutation includes FoundationOne CDx and Cobas® 4800 V600 Mutation Test
II. A Cochrane Review meta-analysis concluded that vemurafenib (Zelboraf) used in combination with cobimetinib (Cotellic) is superior over monotherapy vemurafenib (Zelboraf) in the setting of unresectable or metastatic melanoma.
III. There is limited treatment option for Erdheim-Chester Disease (ECD). The use of vemurafenib (Zelboraf) in ECD was studied in a single-arm, open-label, and multiple cohort basket trial. Given the study design, and the inability to distinguish between the effect of vemurafenib (Zelboraf) and the natural history of ECD, the evidence is considered low quality.

## Investigational or Not Medically Necessary Uses

I. Thyroid cancers (e.g. anaplastic thyroid carcinoma, advanced papillary thyroid cancers with BRAF v600 mutation)
    A. Evidence for the use of vemurafenib (Zelboraf) in the setting of thyroid cancers are limited to phase I trials
II. Non-small cell lung cancer (NSCLC) with BRAF V600E mutation
    A. Evidence for the use of vemurafenib (Zelboraf) in the setting of NSCLC is limited to case studies.
III. Hairy cell leukemia
    A. Evidence for the use of vemurafenib (Zelboraf) in the setting of hairy cell leukemia are limited to phase II trials

## References

1. Zelboraf [Prescribing Information]. South San Francisco, CA: Genetech USA, Inc. November 2017.
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3. Diamond, EL, Subbiah, V, Lockhart, AC, et al. Vemurafenib for BRAF V600-Mutant Erdheim-Chester Disease and Langerhans Cell Histiocytosis: Analysis of Data From the Histology-Independent, Phase 2, Open-label VE-BASKET Study. JAMA oncology. 2018 Mar 1;4(3):384-8. PMID: 29188284
4. Kim K, Cabanillas, M, Lazar A, et al. Clinical Response to Vemurafenib in Patients with Metastatic Papillary Thyroid Cancer Harboring BRAF V600E Mutation. Thyroid. 2013 Oct; 23(10): 1277–1283. DOI: 10.1089/thy.2013.0057
5. Tiacci E, Caroli L, Zaja L, et al. The Chemotherapy-Free Combination of Vemurafenib and Rituximab Produces Deep and Durable Responses in Relapsed or Refractory Hairy Cell Leukemia (HCL) Patients. Blood, 130(Suppl 1), 409. Accessed April 22, 2019. Retrieved from http://www.bloodjournal.org/content/130/Suppl_1/409.
6. Gautschi O, Pauli C, Strobel K, et al. A Patient With BRAF V600E Lung Adenocarcinoma Responding to Vemurafenib. Journal of Thoracic Oncology , Volume 7 , Issue 10 , e23 - e24. DOI: https://doi.org/10.1097/JTO.0b013e3182629903
7. Park J, Lee JO, Stone RM, et al. Acquired Resistance to BRAF Inhibition in Hcl Is Rare and Retreatment with Vemurafenib at Relapse Can Induce High Response Rates: Final Results of a Phase II Trial of Vemurafenib in Relapsed Hcl. Blood 2018 132:392. DOI: https://doi.org/10.1182/blood-2018-99-119949

## Policy Implementation/Update:

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|---|---|
| Date Created | December 2011 |
| Date Effective | December 2011 |
| Last Updated | November 2017 |
| Last Reviewed | 05/2019 |

| Action and Summary of Changes | Date |
|---|---|
| - After review of evidence regarding safety, the removal of split fill management is clinically appropriate.<br>- Updated renewal duration from 3 months to 12 months to align with usual oncolytic renewal approval duration.<br>- Convert criteria format into policy format | 05/2019 |
| Clarified use of concomitant medication | 09/2017 |