

## PRIOR AUTHORIZATION POLICY

**POLICY:** Oncology – Zelboraf Prior Authorization Policy

- Zelboraf<sup>®</sup> (vemurafenib tablets – Genentech/Daiichi Sankyo)

**REVIEW DATE:** 08/14/2024

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### OVERVIEW

Zelboraf, a BRAF inhibitor, is indicated in adults for the following indications:<sup>1</sup>

- **Erdheim-Chester disease**, for treatment of patients with the *BRAF V600* mutation.
- **Melanoma**, for treatment of unresectable or metastatic disease with *BRAF V600E* mutation as detected by an FDA-approved test.

Of note, Cotellic<sup>®</sup> (cobimetinib tablets) is a MEK inhibitor that is indicated to be given in combination with Zelboraf in a similar patient population with melanoma. Zelboraf is not recommended for use in patients with wild-type BRAF melanoma.

### Guidelines

National Comprehensive Cancer Network (NCCN) guidelines support use in multiple cancers.

- **Central Nervous System Cancers:** Guidelines (version 2.2024 – July 25, 2024) recommend a BRAF/MEK inhibitor combination (i.e., Tafinlar<sup>®</sup> [dabrafenib capsules]/Mekinist<sup>®</sup> [trametinib tablets] or Zelboraf/Cotellic) for treatment of *BRAF V600E* activation mutation in the following situations: adjuvant treatment (category 2A) of pilocytic astrocytoma, pleomorphic xanthoastrocytoma, or circumscribed ganglioglioma/neuroglioma/glioneuronal tumor; recurrent or progressive and recurrent glioblastoma (all category 2A).<sup>7</sup> BRAF/MEK combination therapy is also recommended for melanoma with brain metastases. Guidelines for pediatric central nervous system (CNS) cancers (version 1.2024 – February 26, 2024) include targeted therapy with Zelboraf as adjuvant therapy or for recurrent or progressive disease for diffuse high-grade gliomas, if the cancer has a *BRAF V600E* mutation (both category 2A).<sup>8</sup> In the adjuvant setting, Zelboraf is recommended under “other recommended regimens” for age < 3 years with BRAF V600E mutated disease.
- **Hairy Cell Leukemia:** Guidelines (version 2.2024 – April 22, 2024) for hairy cell leukemia list Zelboraf ± rituximab among the treatment options for relapsed or refractory disease and for progressive disease after relapsed/refractory therapy.<sup>3</sup> For initial therapy, Zelboraf + Gazyva (obinutuzumab intravenous infusion) has been added as a category 2A recommendation under “useful in certain circumstances” with a qualifier that it can be considered for patients who are unable to tolerate purine analogs including frail patients and those with active infection (all category 2A).
- **Histiocytic Neoplasms:** Guidelines (version 2.2024 – July 19, 2024) recommend Zelboraf (preferred) or Tafinlar (other recommended regimen) for *BRAF V600E*-mutated Erdheim-Chester disease and for multisystem, pulmonary, or CNS Langerhans cell histiocytosis (all category 2A).<sup>6</sup>
- **Melanoma, Cutaneous:** Guidelines (version 2.2024 – April 3, 2024) for cutaneous disease recommend BRAF/MEK inhibitor combinations among the preferred therapies for first-line and subsequent treatment of metastatic or unresectable melanoma with a *V600*-activating mutation.<sup>2</sup> This combination is also recommended for adjuvant treatment (category 2B). While combination BRAF/MEK inhibition is preferred, if a combination is contraindicated, monotherapy with a BRAF inhibitor is an option, especially in patients who are not appropriate candidates for checkpoint

immunotherapy. Zelboraf + Cotellic + Tecentriq (atezolizumab intravenous infusion) is a recommended combination that is “useful in certain circumstances” (category 2A).

- **Non-Small Cell Lung Cancer:** Guidelines (version 7.2024 – June 26, 2024) list Zelboraf among the first-line options for tumors with a *BRAF* mutation (category 2A), particularly if combination therapy with Tafenlar + Mekinist is not tolerated.<sup>4</sup>
- **Thyroid Carcinoma:** Guidelines (version 3.2024 – June 18, 2024) list Zelboraf as a treatment option (category 2B) if cancer is not amenable to radioiodine treatment, for differentiated thyroid cancer (follicular, oncocytic, and papillary cancer subtypes) with a *BRAF V600* mutation.<sup>5</sup>

## POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Zelboraf. All approvals are provided for the duration noted below.

**Automation:** None.

## RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Zelboraf is recommended in those who meet one of the following criteria:

### FDA-Approved Indications

- 1) **Erdheim-Chester Disease.** Approve for 1 year if the patient meets BOTH of the following (A and B):
  - A) Patient is  $\geq 18$  years of age; AND
  - B) Patient has *BRAF V600* mutation-positive disease.
- 2) **Melanoma.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
  - A) Patient is  $\geq 18$  years of age; AND
  - B) Patient has unresectable, advanced, or metastatic melanoma; AND
  - C) Patient has *BRAF V600* mutation-positive disease.

### Other Uses with Supportive Evidence

- 3) **Central Nervous System Cancer.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
  - A) The medication is being used for ONE of the following (i, ii, or iii):
    - i. Adjuvant treatment of ONE of the following (a, b, c, or d):
      - a) Pilocytic astrocytoma; OR
      - b) Pleomorphic xanthoastrocytoma; OR
      - c) Circumscribed ganglioglioma, or neuroglioma, or glioneuronal tumor; OR
      - d) Pediatric diffuse high-grade glioma; OR
    - ii. Recurrent or progressive disease for ONE of the following (a, b, or c):
      - a) High-grade glioma; OR
      - b) Circumscribed glioma; OR
      - c) Glioblastoma; OR
    - iii. Brain metastases due to melanoma; AND
  - B) Patient has *BRAF V600* mutation-positive disease; AND
  - C) The medication is prescribed in combination with Cotellic (cobimetinib tablets).
- 4) **Hairy Cell Leukemia.** Approve for 1 year if the patient meets BOTH of the following (A and B):

- A) Patient is  $\geq 18$  years of age; AND
  - B) Patient meets ONE of the following (i or ii):
    - i. Patient has tried at least one other systemic therapy for hairy cell leukemia; OR  
Note: Examples of other systemic therapies include cladribine, Nipent (pentostatin injection), rituximab, Intron A (interferon alpha-2b injection).
    - ii. Patient meets BOTH of the following (a and b):
      - a) Patient is unable to tolerate purine analogs (i.e., active infection, frail patients); AND  
Note: Examples of purine analogs are cladribine, Nipent (pentostatin injection).
      - b) Zelboraf is used in combination with Gazyva (obinutuzumab intravenous infusion) as initial therapy.
- 5) **Histiocytic Neoplasm.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):  
Note: For Erdheim-Chester disease, refer to FDA-approved indication.
- A) Patient is  $\geq 18$  years of age; AND
  - B) Patient has Langerhans cell histiocytosis and ONE of the following (i, ii, or iii):
    - i. Multisystem disease; OR
    - ii. Pulmonary disease; OR
    - iii. Central nervous system lesions; AND
  - C) Patient has *BRAF V600* mutation-positive disease.
- 6) **Non-Small Cell Lung Cancer.** Approve for 1 year if the patient meets BOTH of the following (A and B):
- A) Patient is  $\geq 18$  years of age; AND
  - B) Patient has *BRAF V600E* mutation-positive disease.
- 7) **Thyroid Carcinoma, Differentiated.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
- A) Patient is  $\geq 18$  years of age; AND
  - B) Patient has differentiated thyroid carcinoma; AND  
Note: Examples of differentiated thyroid carcinoma include papillary, follicular, and oncocytic carcinoma (formerly Hürthle cell carcinoma).
  - C) Patient has disease that is refractory to radioactive iodine therapy; AND
  - D) Patient has *BRAF* mutation-positive disease.

#### CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Zelboraf is not recommended in the following situations:

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

1. Zelboraf® tablet [prescribing information]. South San Francisco, CA: Genentech; May 2020.
2. The NCCN Melanoma Clinical Practice Guidelines in Oncology (version 2.2024 – April 3, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org/>. Accessed on August 11, 2024.
3. The NCCN Hairy Cell Leukemia Clinical Practice Guidelines in Oncology (version 2.2024 – April 22, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org/>. Accessed on August 11, 2024.
4. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (version 7.2024 – June 26, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org/>. Accessed on August 11, 2024.
5. The NCCN Thyroid Carcinoma Clinical Practice Guidelines in Oncology (version 3.2024 – June 18, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org/>. Accessed on August 11, 2024.
6. The NCCN Histiocytic Neoplasms Clinical Practice Guidelines in Oncology (version 2.2024 – July 19, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org/>. Accessed on August 11, 2024.
7. The NCCN Central Nervous System Cancers Clinical Practice Guidelines in Oncology (version 2.2024 – July 25, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org/>. Accessed on August 11, 2024.
8. The NCCN Pediatric Central Nervous System Cancers Clinical Practice Guidelines in Oncology (version 1.2024 – February 26, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org/>. Accessed on August 11, 2024.
9. The NCCN Drugs & Biologics Compendium. © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org/>. Accessed on August 10, 2024. Search terms: vemurafenib