PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Zelboraf Prior Authorization Policy
- Zelboraf® (vemurafenib tablets – Genentech/Daiichi Sankyo)

REVIEW DATE: 08/14/2024

OVERVIEW

Zelboraf, a BRAF inhibitor, is indicated in adults for the following indications:[1]

- **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® (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® [dabrafenib capsules]/Mekinist® [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 gangliolioma/neuroglioma/glioneuronal tumor; recurrent or progressive and recurrent glioblastoma (all category 2A).[7] 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).[8] 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.[3] 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 histocytosis (all category 2A).[6]
- **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.[2] 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 Tafinlar + Mekinist is not tolerated.[4]
- **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.[5]

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 ≥ 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 ≥ 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 ≥ 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 ≥ 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 ≥ 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 ≥ 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.
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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