PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 08/03/2022

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 1.2022 – June 2, 2022) 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 of pilocytic astrocytoma, pleomorphic xanthoastrocytoma, or ganglioglioma; recurrent or progressive low-grade glioma; oliogdenroglioma, or isocitrate dehydrogenase-2 (*IDH2*)-mutant astrocytoma; and recurrent glioblastoma.[7] BRAF/MEK combination therapy is also recommended for melanoma with brain metastases. Guidelines for pediatric central nervous system (CNS) cancers (version 1.2023 – July 12, 2022) include targeted therapy with Zelboraf as adjuvant therapy or for recurrent or progressive disease, if the cancer has a *BRAF V600E* mutation.[8] In the study cited by NCCN, patients were as young as 3 years of age.
- **Hairy Cell Leukemia:** Guidelines (version 1.2022 – September 8, 2022) 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]
- **Histiocytic Neoplasms**: Guidelines (version 1.2022 – May 20, 2022) recommend Zelboraf (preferred) or Tafinlar (other recommended regimen) for *BRAF V600E*-mutated Erdheim-Chester disease and for multisystem, pulmonary, or CNS Langerhans cell histocytosis.[6]
- **Melanoma, Cutaneous:** Guidelines (version 2.2022 – April 11, 2022) 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] While combination BRAF/MEK inhibition is preferred, if a combination is contraindicated, monotherapy with a BRAF inhibitor is an option. Tafinlar + Mekinist is also recommended 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. If unacceptable toxicity to Tafinlar/Mekinist, other BRAF/MEK combinations can be considered.
- **Non-Small Cell Lung Cancer:** Guidelines (version 3.2022 – March 16, 2022) list Zelboraf among the first-line options for tumors with a *BRAF* mutation, particularly if combination therapy with Tafinlar + Mekinist is not tolerated.[4]

- **Thyroid Carcinoma:** Guidelines (version 2.2022 – May 5, 2022) list Zelboraf as a treatment option if cancer is not amenable to radioiodine treatment, for differentiated thyroid cancer (follicular, Hürthle cell, and papillary cancer subtypes) with a *BRAF V600* mutation.

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 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 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 the following (A, B, C, and D):
   - **A)** Patient is ≥ 3 years of age; AND
   - **B)** The medication is being used for one of the following situations (i, ii, or iii):
     - **i.** Adjuvant treatment of one of the following conditions (a, b, or c):
       - **a)** Pilocytic astrocytoma; OR
       - **b)** Pleomorphic xanthoastrocytoma; OR
       - **c)** Ganglioglioma; OR
     - **ii.** Recurrent or progressive disease for one of the following conditions (a, b, c, or d):
       - **a)** Glioma; OR
       - **b)** Isocitrate dehydrogenase-2 (*IDH2*)-mutant astrocytoma; OR
       - **c)** Oligodendroglioma; OR
       - **d)** Glioblastoma; OR
     - **iii.** Brain metastases due to melanoma; AND
   - **C)** Patient has *BRAF V600* mutation-positive disease; AND
   - **D)** The medication is prescribed in combination with Cotellic (cobimetinib tablets).

4. **Hairy Cell Leukemia.** Approve for 1 year if the patient meets the following (A and B):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has tried at least one other systemic therapy for hairy cell leukemia.
     Note: Examples of other systemic therapies include cladribine, Nipent (pentostatin injection), rituximab, Intron A (interferon alpha-2b injection).

5. **Histiocytic Neoplasm.** Approve for 1 year if the patient meets 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 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 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, or Hürthle cell thyroid cancers.
   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 2.2022 – April 11. 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org/. Accessed on July 30, 2022.
3. The NCCN Hairy Cell Leukemia Clinical Practice Guidelines in Oncology (version 1.2022 – September 8, 2021). © 2021 National Comprehensive Cancer Network. Available at: http://www.nccn.org/. Accessed on July 30, 2022.
4. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (version 3.2022 – March 16, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org/. Accessed on July 30, 2022.
5. The NCCN Thyroid Carcinoma Clinical Practice Guidelines in Oncology (version 2.2022 – May 5, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org/. Accessed on July 30, 2022.
6. The NCCN Histiocytic Neoplasms Clinical Practice Guidelines in Oncology (version 1.2022 – May 20, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org/. Accessed on July 30, 2022.
7. The NCCN Central Nervous System Cancers Clinical Practice Guidelines in Oncology (version 1.2022 – June 2, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org/. Accessed on July 30, 2022.
8. The NCCN Pediatric Central Nervous System Cancers Clinical Practice Guidelines in Oncology (version 1.2023 – July 12, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org/. Accessed on July 30, 2022.