PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 07/15/2020

OVERVIEW

Zelboraf, a BRAF inhibitor, is indicated 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 of Zelboraf in multiple cancers.
- **Melanoma:** Guidelines (version 3.2020 – May 18, 2020) recommend BRAF/MEK inhibitor combinations for first-line (preferred if clinically needed for early response) 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 (Tafinlar® [dabrafenib capsules] or Zelboraf) is a recommended option, particularly if the patient is not a candidate for checkpoint immunotherapy. Following resection of limited metastatic disease with a *BRAF V600*-activating mutation, BRAF/MEK combination therapy is among the treatment options for patients with no evidence of disease. Tafinlar + Mekinist® (trametinib tablets) is also recommended in guidelines 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.
- **Hairy Cell Leukemia:** NCCN guidelines for hairy cell leukemia (version 1.2020 – August 23, 2019) list Zelboraf ± rituximab among the treatment options for relapsed or refractory disease.[3]
- **Non-Small Cell Lung Cancer:** NCCN guidelines (version 6.2020 – June 25, 2020) list Tafinlar + Mekinist among the first-line therapy and subsequent therapy options for tumors with a *BRAF* mutation.[4] NCCN also notes that monotherapy with a BRAF inhibitor (Tafinlar or Zelboraf) is a treatment option when combination therapy is not tolerated.
- **Thyroid Cancer:** Guidelines (version 1.2020 – June 12, 2020) list Tafinlar + Mekinist as a treatment option for metastatic anaplastic thyroid cancer with a *BRAF* mutation.[5] Tafinlar and Zelboraf are also treatment options for the treatment of iodine-refractory 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 3 years unless otherwise noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indications

1. **Erdheim-Chester Disease.** Approve for 3 years if the patient has *BRAF V600* mutation-positive disease.

2. **Melanoma.** Approve Zelboraf for 3 years if the patient meets BOTH of the following (A and B):
   A) Patient has unresectable, advanced, or metastatic melanoma; AND
   B) Patient has *BRAF V600* mutation-positive disease.

Other Uses with Supportive Evidence

3. **Hairy Cell Leukemia.** Approve for 3 years if the 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 injection, Intron A (interferon alpha-2b injection).

4. **Non-Small Cell Lung Cancer.** Approve for 3 years if the patient has *BRAF V600E* mutation-positive disease.

5. **Thyroid Cancer, Differentiated.** Approve Zelboraf for 3 years if the patient meets ALL of the following conditions (A, B, and C):
   A) Patient has differentiated thyroid carcinoma; AND
   Note: Examples of differentiated thyroid carcinoma include papillary, follicular, or Hürthle cell thyroid cancers.
   B) Patient has disease that is refractory to radioactive iodine therapy; AND
   C) 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, oral [prescribing information]. South San Francisco, CA: Genentech USA, Inc.; May 2020.
2. The NCCN Melanoma Clinical Practice Guidelines in Oncology (Version 3.2020 – May 18, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on July 2, 2020.
3. The NCCN Hairy Cell Leukemia Clinical Practice Guidelines in Oncology (Version 1.2020 – August 23, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on July 2, 2020.
4. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (Version 6.2020 – June 15, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on July 2, 2020.
5. The NCCN Thyroid Carcinoma Clinical Practice Guidelines in Oncology (Version 1.2020 – June 12, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on July 2, 2020.