Reference number(s)
1685-A

SPECIALTY GUIDELINE MANAGEMENT

ZELBORAF (vemurafenib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met, and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Zelboraf is indicated for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation as detected by an FDA-approved test.

   Limitation of use: Zelboraf is not indicated for treatment of patients with wild-type BRAF melanoma.

2. Zelboraf is indicated for the treatment of patients with Erdheim-Chester Disease with BRAF V600 mutation.

B. Compendial Uses
1. Non-small cell lung cancer, BRAF V600E mutation-positive
2. Hairy cell leukemia
3. Thyroid carcinoma
   a. Papillary carcinoma
   b. Follicular carcinoma
   c. Hürthle cell carcinoma
4. Glioma, BRAF V600 activating mutation-positive
5. Meningioma, BRAF V600 activating mutation-positive
6. Astrocytoma, BRAF V600 activating mutation-positive
7. Cutaneous melanoma
8. Histiocytic Neoplasms
   a. Erdheim-Chester Disease
   b. Langerhans Cell Histiocytosis

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of BRAF mutation documentation is necessary to initiate the prior authorization review for applicable indications as outlined in Section III.

III. CRITERIA FOR INITIAL APPROVAL

A. Cutaneous Melanoma

Authorization of 12 months may be granted for treatment of cutaneous melanoma with a BRAF V600 activating mutation (e.g., V600E or V600K) in any of the following settings:

1. Unresectable or metastatic disease when used as a single agent or in combination with cobimetinib (Cotellic) with or without atezolizumab (Tecentriq).
2. Adjuvant treatment of resected stage III disease in combination with cobimetinib (Cotellic) when the member has had an unacceptable toxicity to dabrafenib (Tafinlar) in combination with trametinib (Mekinist) or dabrafenib/trametinib are less desirable based on side-effect profiles.
3. Limited resectable local satellite/in-transit recurrent disease in combination with cobimetinib (Cotellic) when the member has had an unacceptable toxicity to dabrafenib (Tafinlar) in combination with trametinib (Mekinist) or dabrafenib/trametinib are less desirable based on side-effect profiles.

B. Central Nervous System Cancer

Authorization of 12 months may be granted for treatment of BRAF V600 mutation-positive (e.g., BRAF V600E or V600K mutation) gliomas, meningiomas, or astrocytomas.

C. Histiocytic Neoplasms

Authorization of 12 months may be granted for treatment of BRAF V600 mutation-positive (e.g., BRAF V600E or V600K mutation) Erdheim-Chester disease or Langerhans cell histiocytosis as a single agent.

D. Non-small Cell Lung Cancer (NSCLC)

Authorization of 12 months may be granted for treatment of BRAF V600E mutation-positive advanced or metastatic NSCLC, as a single agent, if the combination of dabrafenib (Tafinlar) plus trametinib (Mekinist) is not tolerated.

E. Hairy Cell Leukemia

Authorization of 12 months may be granted for treatment of hairy cell leukemia for either of the following:

1. Subsequent therapy as a single agent or in combination with rituximab, or
2. Initial therapy in combination with obinutuzumab for members who are unable to tolerate purine analogs

F. Thyroid Carcinoma

Authorization of 12 months may be granted when all of the following criteria are met:

1. Member has follicular, Hürthle cell, or papillary thyroid carcinoma that is not amenable to radioactive iodine (RAI) therapy.
2. Tumor is positive for BRAF mutation (e.g., BRAF V600E or V600K).

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Zelboraf [package insert]. South San Francisco, CA: Genentech USA, Inc.; May 2020.
2. The NCCN Drugs & Biologics Compendium 2021 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed November 5, 2021.
3. Usubalieva A, Pierson CR, Kavran CA, et al. Primary Meningeal Pleomorphic Xanthoastrocytoma With Anaplastic Features: A Report of 2 Cases, One With BRAFV600E Mutation and Clinical Response to

the BRAF Inhibitor Dabrafenib. Journal of neuropathology and experimental neurology. 2015;74(10):960-969. doi:10.1097/NEN.0000000000000240.

4. Mordechai O, Postovsky S, Vlodavsky E, et al. Metastatic Rhabdoid Meningioma with BRAF V600E Mutation and Good Response to Personalized Therapy: Case Report and Review of the Literature. Pediatric Hematology and Oncology. 2015; 32:3, 207-211, DOI: 10.3109/08880018.2014.936058
5. Lassaletta, A, Guerreiro Stucklin, A, Ramaswamy, V, et al. Profound clinical and radiological response to BRAF inhibition in a 2-month-old diencephalic child with hypothalamic/chiasmatic glioma. Pediatric Blood and Cancer. 2016; 63: 2038-2041. doi:10.1002/pbc.26086.
6. Meletah SK, Pavlick D, Brennan T, et al. Personalized Treatment for a Patient with a BRAF V600E Mutation using Dabrafenib and a Tumor Treatment Fields Device in a High-Grade Glioma Arising from Ganglioglioma. Journal of the National Comprehensive Cancer Network. 2016; 14(11): 1345-1350.
7. National Comprehensive Cancer Network. Thyroid Carcinoma (Version 3.2022). Available at: https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf. Accessed November 14, 2022.