Zelboraf (vemurafenib)

Override(s)	Approval Duration
Prior Authorization Quantity Limit	1 year

Medications	Quantity Limit
Zelboraf (vemurafenib)	May be subject to quantity limit

APPROVAL CRITERIA

Requests for Zelboraf (vemurafenib) may be approved if the following criteria are met:

Individual has a diagnosis of one of the following:

I. Individual has unresectable or metastatic Melanoma (Label, NCCN 1, 2A); **AND**
   A. Individual is using in combination with cobimetinib for disease with BRAF V600 activating mutation;
   OR
   B. Individual is using as a single agent if unacceptable toxicities or intolerable side effect profiles with dabrafenib/trametinib inhibitor combination (NCCN 2A);
   OR
   C. Individual is using as monotherapy for disease with BRAF V600E mutation; **OR**
   D. Individual is using in combination with cobimetinib *and* atezolizumab; **AND**
   E. Used in one of the following ways:
      1. As second-line or subsequent therapy for BRAF V600 activating mutation following progression or intolerance if BRAF/MEK and/or PD(L)-1 checkpoint inhibition not previously used; **OR**
      2. As re-induction therapy If prior therapy consisted of combination BRAF/MEK + PD(L)-1 checkpoint inhibition;

OR

II. Individual has limited resectable stage III cutaneous melanoma (NCCN 2A); **AND**
   A. Individual has either clinical satellite/in-transit metastases or local satellite/in-transit recurrence; **AND**
   B. Individual is using as initial treatment; **AND**
   C. Individual is using in combination with cobimetinib for disease with BRAF V600 activating mutation and unacceptable toxicities or intolerable side effect profiles with dabrafenib/trametinib combination;

OR

III. Recurrent, advanced, or metastatic Non-Small Cell Lung Cancer (NCCN 2A); **AND**
   A. Individual is using as first-line therapy or as subsequent therapy (following progression on first-line therapy with a non-BRAF-targeted regimen); **AND**

B. Individual has a BRAF V600E mutation; **AND**
C. Individual cannot tolerate the combination of dabrafenib plus trametinib;

OR

IV. Histiocytic Neoplasms, including Erdheim-Chester Disease and Langerhans Cell Histiocytosis; **AND**
A. Individual has BRAF V600 mutation; AND
B. Individual is using as a single agent;

OR

V. Relapsed or refractory Hairy cell leukemia (NCCN 2A); **AND**
A. Individual is using as monotherapy; **OR**
B. Individual is using in combination with rituximab (or rituximab biosimilars); **OR**
C. Individual is using in combination with obinutuzumab as initial therapy and unable to tolerate purine analogs including frail individuals and those with active infection;

OR

VI. Central Nervous System Cancer (CNS) (NCCN 2A); **AND**
A. Individual is using in combination with cobimetinib; **AND**
B. Used in one of the following ways;
1. Individual is using for Adult Glioma; **OR**
2. Individual is using for primary CNS cancer (metastatic melanoma with brain metastases); **AND**
C. Individual has BRAF V600E mutation;

OR

VIII. Pediatric Diffuse High-Grade Gliomas (NCCN 2A); **AND**
A. Individual is using in one of the following ways:
1. As adjuvant therapy; **OR**
2. For recurrent or progressive disease; **AND**
B. Individual is using for Pediatric CNS cancer; **AND**
C. Individual has BRAF V600E mutation.

Zelboraf (vemurafenib) may not be used for the following:

I. Individual is using for the treatment of wild-type BRAF melanoma.

Key References:

1. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2023. URL: http://www.clinicalpharmacology.com. Updated periodically.
2. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: October 10, 2023
3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. Hyman DM, Puzanov I, Subbiah V, et al. Vemurafenib in Multiple Nonmelanoma Cancers with BRAF V600 Mutations [published correction appears in N Engl J Med. 2018 Oct 18;379(16):1585]. *N Engl J Med*. 2015;373(8):726-736. Available at https://www.nejm.org/doi/pdf/10.1056/NEJMoa1502309?articleTools=true
5. Kaley T, Touat M, Subbiah V, et al. BRAF Inhibition in BRAFV600-Mutant Gliomas: Results from the VE-BASKET Study. J Clin Oncol. 2018;36(35):3477-3484. Available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6286161/pdf/JCO.2018.78.9990.pdf
6. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2023; Updated periodically.
7. NCCN Clinical Practice Guidelines in Oncology™. © 2023 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on October 10, 2022.
    a. Central Nervous System Cancers. V1.2023. Revised March 24, 2023.
    b. Cutaneous Melanoma. V2.2023. Revised March 10, 2023
    c. Hairy Cell Leukemia. V1.2023. Revised August 30, 2022.
    d. Histiocytic Neoplasms. V1.2023. Revised August 11, 2023
    e. Non-Small Cell Lung Cancer. V3.2023. Revised April 13, 2023.
    f. Pediatric Central Nervous System Cancers. V2.2023. Revised October 31, 2022.
    g. Thyroid Carcinoma. V4.2023. Revised August 16, 2023.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.