

Applicable Drugs: Zelboraf (vemurafenib)

Preferred: N/A

Non-preferred: N/A

Date of Origin: 2/1/2013

Date Last Reviewed / Revised: 7/3/2025

PRIOR AUTHORIZATION CRITERIA

(May be considered medically necessary when criteria I through VI are met)

- I. Documented diagnosis of one of the following conditions A through E and must meet criteria listed under applicable diagnosis:

FDA- Approved Indication(s)

- A. Unresectable or metastatic melanoma
 - 1. Documented BRAF V600E mutation.
- B. Erdheim-Chester Disease
 - 1. Documented BRAF V600E mutation.

Other Uses With Supportive Evidence

- C. Langerhans Cell Histiocytosis
 - 1. Documented BRAF V600E mutation.
- D. Hairy Cell Leukemia
 - 1. Documented incomplete hematologic recovery with indications for treatment present after initial therapy or relapse <2 years or ≥ 2 years.
 - 2. Documented patient not candidate for purine analogs (frail or those with active infections) if being used for initial therapy.
 - 3. Documented progressive disease after relapsed/refractory therapy.
 - 4. Zelboraf may be used in combination with anti-CD20 mAb (obinutuzumab or rituximab) or single agent.
- E. Non-Small Cell Lung Cancer
 - 1. Documented BRAF V600E mutation.
 - 2. Combination of Tafenlar (dabrafenib) + Mekinist (trametinib) is not tolerated.
 - 3. Documented advanced or metastatic disease.
- F. Central Nervous System Cancer
 - 1. Documented BRAF V600E mutation.
 - 2. Documented indication for ONE of the following

- a) Adjuvant treatment if incomplete resection, biopsy, or surgically inaccessible location for ONE of the following
 - (1) Pilocytic astrocytoma
 - (2) Circumscribed ganglioglioma/neuroglioma/glioneuronal tumor
 - (3) Pleomorphic xanthoastrocytoma (grade 2)
- b) Recurrent or progressive disease for ONE of the following
 - (1) WHO grade 1 circumscribed glioma
 - (2) Glioblastoma
 - (3) WHO grade 2 pleomorphic xanthoastrocytoma (PXA)
 - (4) Circumscribed glioma

3. Zelboraf to be used in combination with Cotellic (cobimetinib)

II. Zelboraf to be used as single agent unless otherwise specified above.

III. Minimum age requirement: 18 years old.

IV. Treatment must be prescribed by or in consultation with an oncologist or hematologist.

V. Request is for a medication with the appropriate FDA labeling, or its use is supported by current clinical practice guidelines.

VI. Refer to the plan document for the list of preferred products. If the requested agent is not listed as a preferred product, must have documented treatment failure or contraindication to the preferred product(s).

EXCLUSION CRITERIA

- Patients with wild-type BRAF melanoma
- Pregnancy
- Unable to swallow whole as cannot crush or chew tablets

OTHER CRITERIA

- Use of Zelboraf with strong CYP3A4 inhibitors or inducers should be avoided. Exceptions may be made for higher doses (up to 300 tablets per 30 days) when concomitant use with CYP3A4 inducers (medications that decrease Zelboraf serum concentrations) cannot be avoided (i.e. phenytoin, carbamazepine, rifampin, etc.).

QUANTITY / DAYS SUPPLY RESTRICTIONS

- 240 tablets per 30 days [see under Other Criteria for possible exceptions for higher doses (up to 300 tablets per 30 days)].

APPROVAL LENGTH

- **Authorization:** 12 months
- **Re-Authorization:** An updated letter of medical necessity or progress notes showing current medical necessity criteria are met and does not show evidence of progressive disease.

APPENDIX

N/A

REFERENCES

1. NCCN Clinical Practice Guidelines in Oncology. Cutaneous Melanoma. V2.2025. Updated January 28, 2025. Accessed July 3, 2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cutaneous_melanoma.pdf.
2. NCCN Clinical Practice Guidelines in Oncology. Histiocytic Neoplasms. V1.2025. Updated June 20, 2025. Accessed July 3, 2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/histiocytic_neoplasms.pdf
3. NCCN Clinical Practice Guidelines in Oncology. Non-Small Cell Lung Cancer. V6.2025. Updated July 2, 2025. Accessed July 3, 2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf
4. NCCN Clinical Practice Guidelines in Oncology. Hairy Cell Leukemia. V1.2025. Updated September 26, 2024. Accessed July 3, 2025. Available at: www.nccn.org/professionals/physician_gls/pdf/hairy_cell.pdf.
5. Diamond EL, et. al., Consensus guidelines for the diagnosis and clinical management of Erdheim-Chester disease. Blood. 2014;124(4):483-92. doi: 10.1182/blood-2014-03-561381.
6. Zelboraf. Prescribing Information. Genentech; May 2020. Accessed July 3, 2025. Available at: http://www.gene.com/download/pdf/zelboraf_prescribing.pdf.
7. NCCN Clinical Practice Guidelines in Oncology. Central Nervous System Cancers. V1.2025. Updated June 3, 2025. Accessed July 3, 2025. Available at: www.nccn.org/professionals/physician_gls/pdf/cns.pdf.

DISCLAIMER: Medication Policies are developed to help ensure safe, effective and appropriate use of selected medications. They offer a guide to coverage and are not intended to dictate to providers how to practice medicine. Refer to Plan for individual adoption of specific Medication Policies. Providers are expected to exercise their medical judgement in providing the most appropriate care for their patients.