UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2024 P 1119-12
Program	Prior Authorization/Notification
Medication	Zelboraf® (vemurafenib)
P&T Approval Date	8/2012, 7/2013, 5/2014, 5/2015, 5/2016, 3/2017, 3/2018, 3/2019, 3/2020, 3/2021, 3/2022, 3/2023, 3/2024
Effective Date	6/1/2024

1. Background:

Zelboraf (vemurafenib) is a kinase inhibitor indicated for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation as detected by an FDA-approved test. It is also indicated for the treatment of patients with Erdheim-Chester Disease with BRAF V600 mutation. Zelboraf is not recommended for use in patients with wild-type BRAF melanoma.[1]

The National Cancer Comprehensive Network (NCCN) guideline recommends use of Zelboraf in combination with Cotellic (cobimetinib) for treatment of central nervous system (CNS) cancer and metastatic or unresectable melanoma with a BRAF V600 mutation (or as a single agent if BRAF/MEK inhibitor combination therapy is contraindicated). Zelboraf is also recommended for the treatment of hairy cell leukemia, non-small cell lung cancer (NSCLC), Langerhans cell histiocytosis (LCH), and follicular, Hürthle cell, and papillary thyroid carcinomas with a BRAF mutation.[2]

Information on FDA-approved tests for the detection of BRAF V600 mutations in melanoma may be found at: http://www.fda.gov/CompanionDiagnostics.[1]

Coverage Information:

Members will be required to meet the criteria below for coverage. For members under the age of 19 years, the prescription will automatically process without a coverage review.

Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances. Some states also mandate usage of other Compendium references. Where such mandates apply, they supersede language in the benefit document or in the notification criteria.

2. Coverage Criteria[a]:

A. Patients less than 19 years of age

1. **Zelboraf** will be approved based on the following criterion:

   a. Patient is less than 19 years of age

   Authorization will be issued for 12 months.

B. Melanoma

1. **Initial Authorization**

a. **Zelboraf** will be approved based on **both** of the following criteria:

(1) **One** of the following diagnoses:

(a) Unresectable melanoma

(b) Metastatic melanoma

-AND-

(2) Patient is positive for BRAFV600 mutation

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Zelboraf** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Zelboraf therapy

Authorization will be issued for 12 months.

C. Central Nervous System (CNS) Cancers

1. **Initial Authorization**

a. **Zelboraf** will be approved based on **all** of the following criteria:

(1) **One** of the following:

(a) **Both** of the following:

i. Patient has metastatic brain lesions

-AND-

ii. Zelboraf is active against primary tumor (melanoma)

-OR-

(b) **Both** of the following:

i. Diagnosis of Glioma

-AND-

ii. **One** of the following:
- Incomplete resection, biopsy, or surgically inaccessible location
- Disease is recurrent or progressive

-AND-

(2) Cancer is positive for BRAF V600E mutation

-AND-

(3) Used in combination with Cotellic (cobimetinib)

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Zelboraf** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Zelboraf therapy

Authorization will be issued for 12 months.

D. Hairy Cell Leukemia

1. **Initial Authorization**

a. **Zelboraf** will be approved based on the following diagnosis:

(1) Diagnosis of hairy cell leukemia

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Zelboraf** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Zelboraf therapy

Authorization will be issued for 12 months.

E. Non-Small Cell Lung Cancer (NSCLC)

1. **Initial Authorization**

a. **Zelboraf** will be approved based on **all** of the following:

(1) Diagnosis of non-small cell lung cancer (NSCLC)

-AND-

(2) Disease is **one** of the following:

(a) Metastatic
(b) Advanced
(c) Recurrent

-AND-

(3) Cancer is positive for BRAF V600E mutation

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Zelboraf** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Zelboraf therapy

Authorization will be issued for 12 months.

F. Histiocytic Neoplasms

1. **Initial Authorization**

a. **Zelboraf** will be approved based on **both** of the following:

(1) Diagnosis of **one** of the following:

(a) Erdheim-Chester Disease
(b) Langerhans Cell Histiocytosis

-AND-

(2) Cancer is positive for BRAF V600 mutation

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Zelboraf** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Zelboraf therapy

Authorization will be issued for 12 months.

G. Thyroid Cancer

1. **Initial Authorization**

a. **Zelboraf** will be approved based on **all** of the following:

(1) Diagnosis of **one** of the following:

(a) Follicular carcinoma
(b) Oncocyticcarcinoma
(c) Papillary carcinoma

-AND-

(2) **One** of the following:

(a) Unresectable locoregional recurrent disease
(b) Metastatic disease
(c) Persistent disease

-AND-

(3) **One** of the following:

(a) Patient has symptomatic disease
(b) Patient has progressive disease

-AND-

(4) Disease is refractory to radioactive iodine

-AND-

(5) Cancer is positive for BRAF V600 mutation

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Zelboraf** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Zelboraf therapy

Authorization will be issued for 12 months.

H. NCCN Recommended Regimens

The drug has been recognized for treatment of the cancer indication by The National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium with a Category of Evidence and Consensus of 1, 2A, or 2B

Authorization will be issued for 12 months.

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply.

3. Additional Clinical Rules:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.
- Supply limits may be in place.

4. References:

1. Zelboraf [package insert]. South San Francisco, CA: Genentech, Inc.; May 2020.
2. The NCCN Drugs and Biologics Compendium (NCCN Compendium™). Available at www.nccn.org. Accessed February 6, 2024.

Program	Prior Authorization/Notification - Zelboraf (vemurafenib)
Change Control	
5/2014	Annual review with no change to coverage.
5/2015	Annual review. Added criteria for CNS cancer and NSCLC. Updated background and references. Increased authorization to 12 months.
5/2016	Annual review. Removed incompletely resected or recurrent from melanoma. Updated background and references.
3/2017	Annual review. Changed Member to Patient in criterion. Updated references.
3/2018	Annual review. Updated background and criteria to include new indication for Erdheim-Chester Disease and NCCN recommended off-label use in BRAF mutation positive colon, rectal, and thyroid cancer. Updated references.
3/2019	Annual review. Updated criteria for NCCN recommended use in CNS cancer. Updated background and references.
3/2020	Annual review. Added general NCCN recommendations for use criteria. Updated references.
3/2021	Annual review. Updated coverage criteria for CNS cancer per NCCN recommendations. Removed coverage criteria for colon and rectal cancer. These recommendations were not included in current version of NCCN guidelines for colon or rectal cancer. Updated references.
3/2022	Annual review. Updated background and coverage criteria for Langerhans cell histiocytosis per NCCN recommendations.
3/2023	Annual review. Updated background and CNS coverage criteria per NCCN recommendations. Updated reference. Added state mandate footnote.
3/2024	Annual review. Updated nomenclature under Thyroid carcinoma from Hurthle cell to oncocytic with no change to clinical intent. Updated reference.