Clinical Policy: Vemurafenib (Zelboraf)

Reference Number: ERX.SPA.85
Effective Date: 03.01.14
Last Review Date: 02.22
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Vemurafenib (Zelboraf®) is a kinase inhibitor.

FDA Approved Indication(s)
Zelboraf is indicated for the treatment of patients with:
- Unresectable or metastatic melanoma with BRAF V600E mutation as detected by an FDA-approved test
- Erdheim-Chester disease with BRAF V600 mutation

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

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Zelboraf is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Melanoma (must meet all)**:**
1. Diagnosis of recurrent, lymph node positive, unresectable, or metastatic melanoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. For Zelboraf requests, member must use vemurafenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. Positive for a BRAF V600 mutation;
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 1,920 mg (8 tablets) per day.
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Commercial – Length of Benefit
Medicaid – 6 months

B. Histiocytic Neoplasms (must meet all)**:**
1. Diagnosis of one of the following (a or b):
   a. Erdheim-Chester disease;
   b. Langerhans cell histiocytosis (off-label);
2. Prescribed by or in consultation with a hematologist or oncologist;
3. Age ≥ 18 years;
4. For Zelboraf requests, member must use vemurafenib, if available, unless contraindicated or clinically significant adverse effects are experienced;

5. Positive for a BRAF V600 mutation;
6. Request meets one of the following (a or b):
   a. Dose does not exceed 1,920 mg (8 tablets) per day.
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration:
Commercial – Length of Benefit
Medicaid – 6 months

C. Non-Small Cell Lung Cancer (off-label) (must meet all)**:**
1. Diagnosis of non-small cell lung cancer (NSCLC);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. For Zelboraf requests, member must use vemurafenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. Positive for a BRAF V600E mutation;
6. Failure of Tafinlar® and Mekinist®, unless contraindicated or clinically significant adverse effects are experienced;*
   **Prior authorization may be required for Tafinlar and Mekinist*
7. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*
   **Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Commercial – Length of Benefit
Medicaid – 6 months

D. Hairy Cell Leukemia (off-label) (must meet all)**:**
1. Diagnosis of hairy cell leukemia;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. For Zelboraf requests, member must use vemurafenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. Prescribed as subsequent therapy for relapsed or refractory disease;
6. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*
   **Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Commercial – Length of Benefit
Medicaid – 6 months

E. Thyroid Carcinoma (off-label) (must meet all)**:**
1. Diagnosis of progressive or symptomatic papillary, follicular or Hurthle cell carcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. For Zelboraf requests, member must use vemurafenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. Positive for a BRAF mutation;
6. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*
   **Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Commercial – Length of Benefit
Medicaid – 6 months

F. Central Nervous System Cancers (off-label) (must meet all)**:**
1. Diagnosis of one of the following (a-f):
   a. Pilocytic astrocytoma;
   b. Pleomorphic xanthoastrocytoma;
   c. Ganglioglioma;
   d. Anaplastic glioma;
   e. Glioblastoma;
   f. Adult low-grade (grade 1 or 2) glioma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Prescribed in combination with Cotellic®;
5. For Zelboraf requests, member must use vemurafenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Positive for a BRAF V600E mutation;
7. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*
   **Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Commercial – Length of Benefit
Medicaid – 6 months

G. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Zelboraf for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For Zelboraf requests, member must use vemurafenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed 1920 mg (8 tablets) per day;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence)*.
   **Prescribed regimen must be FDA-approved or recommended by NCCN (exception: Erdheim-Chester disease).*

Approval duration:
Commercial – Length of Benefit
Medicaid – 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents;

B. Wild-type BRAF disease.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
NCCN: National Comprehensive Cancer Network
NSCLC: non-small cell lung cancer

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Tafinlar (dabrafenib)	NSCLC: 150 mg PO QD	300 mg/day
Mekinist (trametinib)	NSCLC: 2 mg PO QD	2 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
None reported

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Melanoma	960 mg PO BID	1,920 mg/day
Erdheim-Chester disease	960 mg PO BID	1,920 mg/day

VI. Product Availability

Tablet: 240 mg

VII. References

1. Zelboraf Prescribing information. South San Francisco, CA: Genentech USA, Inc.; May 2020. Available at: www.zelboraf.com. Accessed November 9, 2021.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed November 9, 2021.
3. National Comprehensive Cancer Network. Central Nervous System Cancers Version 2.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf. Accessed November 9, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q18 annual review: Converted to newest template. Added Erdheim-Chester disease as a new FDA-approved indication. Added minimum dose requirement of 960 mg/day for brain metastases and thyroid carcinoma. Added off-label usages per NCCN (non-small cell lung cancer, hairy cell leukemia, thyroid carcinoma, brain metastases). Approval durations modified to length of benefit.	12.12.17	02.18
1Q 2019 annual review: age changed from 15 to 18 years per PI; melanoma brain metastasis moved under melanoma criteria set and mutation changed from BRAF V600E to V600 per NCCN; hematologist added as specialist for hairy cell leukemia and failure of specific drugs replaced with Zelboraf as subsequent therapy given additional NCCN recommended uses; for thyroid carcinoma, required failure of lenvatinib and sorafenib removed as they are	11.13.18	02.19

Reviews, Revisions, and Approvals	Date	P&T Approval Date
not labeled for the BRAF mutation; CRC off-label use added; references reviewed and updated.		
1Q 2020 annual review: melanoma CNS metastasis no longer an alternative to the required mutation per NCCN 2B rating; added Medicaid line of business with 6/12 month approval durations; references reviewed and updated.	11.19.19	02.20
1Q 2021 annual review: oral oncology generic redirection language added; recurrent/lymph node positive added to melanoma per NCCN; progressive/symptomatic added to thyroid carcinoma per NCCN; astrocytoma/oligodendroglioma use added per NCCN; CRC removed per NCCN; references reviewed and updated.	11.06.20	02.21
1Q 2022 annual review: anaplastic glioma, adult low-grade glioma, and glioblastoma use in combination with Cotellic added per NCCN 2A rating and I.A.F. renamed central nervous system cancers; added Langerhans cell histiocytosis per NCCN 2A rating and included under renamed histiocytic neoplasms to combine with Erdheim-Chester disease; clarified oral oncology generic redirection language to “must use”; references reviewed and updated.	11.09.21	02.22

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.