Clinical Policy: Vemurafenib (Zelboraf)

Reference Number: CP.PHAR.91
Effective Date: 11.01.11
Last Review Date: 05.22
Line of Business: Commercial, HIM, 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
- Patients with 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 (including such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® 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:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less
Legacy Wellcare – 12 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*).

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

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less
Legacy Wellcare – 12 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:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less
Legacy Wellcare – 12 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:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less
Legacy Wellcare – 12 months

E. Thyroid Carcinoma (off-label) (must meet all)**:**
1. Diagnosis of progressive or symptomatic differentiated thyroid carcinoma (i.e., 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:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less
Legacy Wellcare – 12 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:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

Legacy Wellcare – 12 months

G. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit, 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:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less
Legacy Wellcare – 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents;

B. Patients with 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 for all relevant lines of business 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

Tablets: 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: Policies combined for Centene Medicaid, Marketplace and Commercial lines of business. Added oncologist and age limit requirements for the melanoma indication. Added off-label usages per NCCN recommendations, including new coverage for thyroid carcinoma and brain metastases (2A recommendations). Changed Approval Durations for Medicaid and HIM from 3/6 months to 6/12 months.	12.12.17	02.18
Added Erdheim-Chester disease as a new FDA-approved indication	12.12.17	02.18
1Q 2019 annual review; age changed from 15 to 18 years per PI; FDA approved test restriction removed; melanoma brain metastasis moved	11.13.18	02.19

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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 not labeled for the BRAF mutation; CRC off-label use added; references reviewed and updated.		
1Q 2020 annual review: removed HIM disclaimer for HIM NF drugs; melanoma CNS metastasis no longer an alterantive to the required mutation per NCCN 2B rating; 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 to HIM.PHAR.21 revised to HIM.PA.154; 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"; added legacy Wellcare auth durations (WCG.CP.PHAR.91 to retire); references reviewed and updated.	11.09.21	02.22
Revised approval duration for Commercial line of business from length of benefit to 12 months or duration of request, whichever is less	01.20.22	05.22

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage

decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.