Clinical Policy: Vemurafenib (Zelboraf)

Reference Number: CP.PHAR.91
Effective Date: 11.01.11
Last Review Date: 02.25
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. Positive for a BRAF V600 mutation;
5. For Zelboraf requests, member must use generic vemurafenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
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

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. Positive for a BRAF V600 mutation;
5. For Zelboraf requests, member must use generic vemurafenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
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

C. Non-Small Cell Lung Cancer (off-label) (must meet all)**:**
1. Diagnosis of recurrent, advanced, or metastatic non-small cell lung cancer (NSCLC);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Positive for a BRAF V600E mutation;
5. Failure of Tafinlar® and Mekinist® unless contraindicated or clinically significant adverse effects are experienced;*

   **Prior authorization may be required for Tafinlar and Mekinist*
6. For Zelboraf requests, member must use generic vemurafenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
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

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. Prescribed as one of the following (a, b, or c):
   a. For members with indications for treatment who are unable to tolerate purine analogs;
   b. If Zelboraf was not previously given: For those with an incomplete response or who relapse within two years of complete response following initial treatment with cladribine or pentostatin;
   c. Subsequent therapy for relapsed or refractory disease (if not previously given);

5. For Zelboraf requests, member must use generic vemurafenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
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

E. Adult Central Nervous System Cancers (off-label) (must meet all)**:**
1. Diagnosis of one of the following (a-e):
   a. Pilocytic astrocytoma;
   b. Pleomorphic xanthoastrocytoma (grade 2);
   c. Ganglioglioma/neuroglioma/glioneuronal tumor;
   d. Glioblastoma;
   e. Circumscribed glioma or H3-mutated high-grade glioma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Positive for a BRAF V600E mutation;
5. Prescribed in combination with Cotellic®;
6. For Zelboraf requests, member must use generic vemurafenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
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

F. Pediatric Central Nervous System Cancers (off-label) (must meet all)**:**
1. Diagnosis of diffuse high-grade glioma unless any of the following (a or b):
   a. Diffuse midline glioma, H3 K27-altered or pontine location;
   b. Oligodendroglioma, IDH-mutant, and 1p/19q co-deleted or astrocytoma IDH-mutant;
2. Prescribed by or in consultation with an oncologist;
3. Age ≤ 18 years;
4. Positive for a BRAF V600E mutation;
5. For Zelboraf requests, member must use generic vemurafenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
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

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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 generic 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 1,920 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

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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. Members 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, 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 October 25, 2024.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed December 3, 2024.
3. National Comprehensive Cancer Network. Melanoma: Cutaneous Version 3.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cutaneous_melanoma.pdf. Accessed December 3, 2024.
4. National Comprehensive Cancer Network. Histiocytic Neoplasms Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/histiocytic_neoplasms.pdf. Accessed December 3, 2024.
5. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer Version 11.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed December 3, 2024.
6. National Comprehensive Cancer Network. Central Nervous System Cancers Version 3.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf. Accessed December 3, 2024.
7. National Comprehensive Cancer Network. Pediatric Central Nervous System Cancers Version 1.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ped_cns.pdf. Accessed December 3, 2024.
8. National Comprehensive Cancer Network. Thyroid Carcinoma Version 4.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf. Accessed December 3, 2024.
9. National Comprehensive Cancer Network. Hairy Cell Leukemia Version 1.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hairy_cell.pdf. Accessed December 3, 2024.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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	11.09.21	02.22

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Wellcare auth durations (WCG.CP.PHAR.91 to retire); references reviewed and updated.		
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
Template changes applied to other diagnoses/indications.	10.12.22	
1Q 2023 annual review: no significant changes; per NCCN updated the types of recommended off-label hairy cell leukemia and adult CNS tumors, and added coverage for off-label pediatric CNS cancers; Legacy Wellcare approval durations consolidated with Medicaid and HIM to 6 months; references reviewed and updated.	11.22.22	02.23
1Q 2024 annual review: no significant changes; per NCCN guidelines, clarified that use of Zelboraf in NSCLC is only for those with recurrent, advanced, or metastatic disease, clarified that specifically grade 2 pleomorphic xanthoastrocytoma is recommended, expanded use in brain metastases to include those with extensive metastases, clarified nomenclature of Hurthle cell carcinoma to oncocytic carcinoma; references reviewed and updated.	11.28.23	02.24
1Q 2025 annual review: per NCCN guidelines added coverage for neuroglioma and glioneuronal tumor as category 2A-supported indications, updated the types of gliomas to circumscribed gliomas and H3-mutated high-grade glioma, removed coverage of the following conditions as not NCCN-supported (oligodendroglioma, astrocytoma), removed coverage of the following conditions that have category 2B recs (thyroid carcinoma, brain metastases); references reviewed and updated.	12.03.24	02.25

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.