Clinical Policy: Vemurafenib (Zelboraf)

Reference Number: CP.PHAR.91
Effective Date: 11/11
Last Review Date: 03/17

Coding Implications
Revision Log

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

Description
The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for vemurafenib (Zelboraf®).

Policy/Criteria
It is the policy of health plans affiliated with Centene Corporation® that Zelboraf is **medically necessary** when one of the following criteria are met:

I. Initial Approval Criteria

A. Melanoma (must meet all):

1. Diagnosis of unresectable or metastatic melanoma with BRAF V600E mutation as detected by an FDA-approved test;
2. Prescribed dose of Zelboraf is ≥ 480 mg but ≤ 960 mg twice daily.

Approval duration: 3 months

B. Other diagnoses/indications: Refer to CP.PHAR.57 - Global Biopharm Policy.

II. Continued Approval

A. Melanoma (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member is responding positively to therapy;
3. Prescribed dose of Zelboraf is ≥ 480 mg but ≤ 960 mg twice daily.

Approval duration: 6 months

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to CP.PHAR.57 - Global Biopharm Policy**.**

Background
Description/Mechanism of Action:
Vemurafenib is a low molecular weight, orally available inhibitor of some mutated forms of BRAF serine-threonine kinase, including BRAF V600E. Vemurafenib also inhibits other kinases *in vitro* such as CRAF, ARAF, wild-type BRAF, SRMS, ACK1, MAP4K5, and FGR at similar concentrations. Some mutations in the BRAF gene including V600E result in constitutively

activated BRAF proteins which can cause cell proliferation in the absence of growth factors that would normally be required for proliferation. Vemurafenib has anti-tumor effects in cellular and animal models of melanomas with mutated BRAF V600E.

Formulations:
Zelboraf oral tablets: 250 mg

FDA Approved Indications:
Zelboraf is a kinase inhibitor/oral tablet formulation indicated for:

- Treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation as detected by an FDA-approved test.

Limitations of use:

- Zelboraf is not indicated for treatment of patients with wild-type BRAF melanoma.

Appendices
Appendix A: Abbreviation Key
BRAF: B-Raf Proto-Oncogene

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
N/A	

Reviews, Revisions, and Approvals	Date	Approval Date
No clinical changes.	12/12	12/12
Converted embedded SGM document into Centene policy	08/13	
Appendix A added. Dosing added to the algorithm References updated	02/14	03/14
Background updated Efficacy information included Appendix B added with reference added to algorithm References updated	1/15	03/15
Policy converted to new template. Criteria: documentation requests removed; added age criteria; added indication for administration with cobimetinib; added severe hypersensitivity and dermatological reaction to contraindications; removed QT monitoring requirement; removed general question regarding patient response to Zelboraf.	02/16	03/16

Reviews, Revisions, and Approvals	Date	Approval Date
Appendices removed – required information placed directly into criteria.		
Age restriction removed. Wild type BRAF melanoma is removed as a limitation. Safety criteria were removed that did not either represent contraindications or black box warnings not covered by a REMS program; provide specific lab/imaging parameters that must be met prior to initiation of therapy; or can be diagnosed/ruled out with a single test.	02/17	03/17

References

1. Zelboraf prescribing information. South San Francisco, CA: Genentech USA, Inc.; August 2016. Available at https://www.gene.com/download/pdf/zelboraf_prescribing.pdf. Accessed February 22, 2017.
2. Vemurafenib. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at NCCN.org. Accessed February 22, 2017.
3. Melanoma (Version 1.2017). In: National Comprehensive Cancer Network Guidelines. Available at NCCN.org. Accessed February 22, 2017.

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.

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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.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.