Clinical Policy: Vemurafenib (Zelboraf)

Reference Number: PA.CP.PHAR.91
Effective Date: 01/18
Last Review Date: 07/18

Coding Implications
Revision Log

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

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
It is the policy of Pennsylvania Health and Wellness 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;
2. Positive for the b-Raf serine-threonine kinase (BRAF) V600E mutation as detected by an FDA-approved test;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 15 years;
5. Dose does not exceed 960 mg twice daily (4 tablets/day).

Approval duration: 6 months

B. Erdheim-Chester Disease (must meet all)**:**

1. Diagnosis of Erdheim-Chester Disease;
2. Positive for the BRAF V600 mutation as detected by an FDA-approved test;
3. Prescribed by or in consultation with a hematologist or oncologist;
4. Age ≥ 15 years;
5. Dose is does not exceed 960 mg twice daily (4 tablets/day).

Approval duration: 6 months

C. Non-Small Cell Lung Cancer (off-label) (must meet all)**:**

1. Diagnosis of non-small cell lung cancer;
2. Positive for the BRAF V600E mutation as detected by an FDA-approved test;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 15 years;

5. Documentation supports failure of or presence of clinically significant adverse effects or contraindication to dabrafenib and trametinib;
   **dabrafenib and trametinib require PA*
6. Request meets one of the following (a or b):
   a. Dose does not exceed 960 mg twice daily (4 tablets/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: 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;
3. Age ≥ 15 years;
4. Documentation supports failure of or presence of clinically significant adverse effects or contraindication to purine analog therapy (e.g., pentostatin, cladribine);
5. Request meets one of the following (a or b):
   a. Dose does not exceed 960 mg twice daily (4 tablets/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: 6 months

E. Thyroid Carcinoma (off-label) (must meet all)**:**

1. Diagnosis of papillary carcinoma, follicular carcinoma, or Hurthle cell carcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 15 years;
4. Documentation supports failure of or presence of clinically significant adverse effects or contraindication to lenvatinib and sorafenib;
5. Dose is ≥ 960 mg/day;
6. Request meets one of the following (a or b):
   a. Dose does not exceed 960 mg twice daily (4 tablets/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: 6 months

F. Brain Metastases (off-label) (must meet all):

1. Diagnosis of brain metastases;
2. Patient has a primary diagnosis of melanoma against which Zelboraf was active;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 15 years;
5. Dose is ≥ 960 mg/day;
6. Request meets one of the following (a or b):
   a. Dose does not exceed 960 mg twice daily (4 tablets);
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

Approval duration: 6 months

G. Other diagnoses/indications: Refer to PA.CP.PMN.53 Policy.

II. Continued Approval

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):
    a. New dose does not exceed 1920 mg/day;
    b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies; or
2. Refer to PA.CP.PMN.53

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: 240 mg

- 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
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 from 3/6 months to 6/12 months. Added Erdheim-Chester disease as a new FDA-approved indication. References reviewed and updated.	02/18	

References

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8. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer Version 1.2018. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed November 17, 2017.
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