PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 3/13/2012
LAST REVIEW DATE: 2/17/2022
LAST CRITERIA REVISION DATE: 2/17/2022
ARCHIVE DATE:

ZELBORAF® (vemurafenib) oral tablet

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

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Criteria:

- **Criteria for initial therapy:** Zelboraf (vemurafenib) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Oncologist
  2. Individual is 18 years of age or older
  3. A confirmed diagnosis of **ONE** of the following:
     a. Unresectable or metastatic melanoma with a BRAF V600E mutation
     b. Erdheim-Chester Disease with BRAF V600 mutation
     c. Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A
  4. Confirmation the individual is negative for wild-type BRAF melanoma
  5. **ALL** of the following baseline tests have been completed before initiation of treatment:
     a. FDA-approved test confirming the presence of BRAF V600E mutation in tumor specimens
     b. Electrocardiogram (ECG)
     c. Eastern Cooperative Oncology Group (ECOG) Performance Status of 0-1
  6. Will not be used in a patient with severe renal impairment
  7. Will not be used in a patient with moderate or severe hepatic impairment
  8. There are no significant interacting drugs

  Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Zelboraf (vemurafenib) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Oncologist
  2. Individual's condition has responded while on therapy
     a. Response is defined as:
        i. Documented evidence of efficacy, disease stability and/or improvement
        ii. No evidence individual has developed any significant unacceptable adverse drug reactions that may exclude continued use
  3. Requested dose is at least 480 mg twice daily

ZELBORAF® (vemurafenib) oral tablet

4. Individual has been adherent with the medication

5. Individual has not developed any significant level 4 adverse drug effects that may exclude continued use
    a. Significant adverse effect such as:
        i. Stevens-Johnson syndrome or toxic epidermal necrolysis or drug reaction with eosinophilia and systemic symptoms (DRESS)
        ii. QT prolongation > 500 ms and an increase of > 60 ms from baseline
        iii. Hepatotoxicity
        iv. Dupuytren contracture or plantar fascial fibromatosis
        v. Any moderate or severe reaction that does not improve after dose modification
        vi. Any first occurrence or recurrence of a life-threatening reaction

6. Will not be used in a patient with severe renal impairment

7. Will not be used in a patient with moderate or severe hepatic impairment

8. There are no significant interacting drugs

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

    1. **Off-Label Use of Non-cancer Medications**

    2. **Off-Label Use of Cancer Medications**

Description:

Zelboraf® (vemurafenib) is indicated for the treatment of patients with Erdheim-Chester Disease with BRAF V600 mutation; and for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation positive as detected by an FDA-approved test such as the cobas 4800 BRAF V600 Mutation Test or other FDA-approved test. The drug is not recommended for use in patients with wild-type BRAF melanoma. Confirmation of BRAF V600E mutation-positive melanoma as detected by an FDA-approved test is required for selection of patients for Zelboraf® therapy because these are the only patients that have been studied and for whom benefit has been shown. Zelboraf® is a low molecular weight, orally available, inhibitor of some mutated forms of BRAF serine-threonine kinase; including BRAF V600E that is able to block the function of the V600E mutated BRAF protein.

Melanoma is the less common, but more serious type of skin cancer that originates in the skin's pigment-producing cells known as melanocytes. When melanoma is diagnosed early, it is generally treatable. However, when it becomes metastatic, it is the deadliest and most aggressive form of skin cancer and is the leading cause of death from skin disease. The BRAF protein is normally involved in regulating cell growth but is mutated in about half of the patients with late-stage melanomas. The protein plays a key role in normal cell growth and

survival, mutations such as BRAF V600E result in constant growth signals which cause cell proliferation in the absence of growth factors that would normally be required for proliferation.

Definitions:

National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTC-AE):

Grade 1: Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated.

Grade 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age appropriate instrumental activities of daily living (ADL).

Grade 3: Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL.

Grade 4: Life-threatening consequences; urgent intervention indicated.

Grade 5: Death related to adverse event.

Activities of daily living (ADL):

Instrumental ADL: preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.

Self-care ADL: bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not bedridden.

Resources:

Zelboraf (vemurafenib) product information, revised by Genentech, Inc. 05-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed December 02, 2021.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Melanoma: Cutaneous Version 2.2021 – Updated February 19, 2021. Available at https://www.nccn.org. Accessed November 29,2021.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Histiocytic Neoplasms Version 2.2021 – Updated September 08, 2021. Available at https://www.nccn.org. Accessed December 02, 2021.

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.