BlueCross BlueShield of Arizona
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PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 5/14/14**
SECTION: DRUGS	**LAST REVIEW DATE: 8/02/18**
	LAST CRITERIA REVISION DATE: 8/02/18
	ARCHIVE DATE:

TAFINLAR® (dabrafenib mesylate) oral capsule

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.**

TAFINLAR® (dabrafenib mesylate) oral capsule (cont.)

Criteria:

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

1. Prescriber is an Oncologist

2. Individual is 18 years of age or older

3. A confirmed diagnosis of **ONE** of the following:
   - Melanoma with **ONE** of the following:
     - Single agent treatment of unresectable or metastatic melanoma with BRAF mutation V600E disease
     - In combination therapy with trametinib as treatment of unresectable or metastatic melanoma with BRAF mutation V600E or V600K disease in an individual who also fulfills **ALL** of the criteria for trametinib [See Mekinist (trametinib) coverage guidelines]
     - In combination with tramatinib, as adjuvant treatment of melanoma with BRAF V600E or V600K mutation disease and involvement of lymph nodes(s) following complete resection, in an individual who also fulfills **ALL** of the criteria for trametinib [See Mekinist (trametinib) coverage guidelines]
   - Metastatic non-small cell lung cancer (NSCLC) with BRAF V600E mutation used in combination therapy with trametinib in an individual who also fulfills **ALL** of the criteria for trametinib [See Mekinist (trametinib) coverage guidelines]
   - Locally advanced or metastatic anaplastic thyroid cancer (ATC) with BRAF V600E mutation disease and who has no satisfactory locoregional treatment options, in combination with tramatinib in an individual who also fulfills **ALL** of the criteria for trametinib [See Mekinist (trametinib) coverage guidelines]

4. There is confirmation individual does not have wild-type BRAF melanoma or wild-type BRAF NSCLC, or wild-type BRAF ATC

5. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring as clinically appropriate:
   - An FDA-approved test confirming the presence of BRAF V600E or V600K mutation
   - Comprehensive metabolic panel
   - Assessment of left ventricular ejection fraction by echocardiogram or multi-gated acquisition scan

6. Will not be used in a patient with moderate to severe hepatic impairment

7. Will not be used in a patient with severe renal impairment (GFR $\leq$ 30 mL/min/1.73 m^2)

TAFINLAR® (dabrafenib mesylate) oral capsule (cont.)

8. Woman patient of child bearing potential should use effective non-hormonal contraception during and for 2 weeks after therapy

9. Woman patient who is breast feeding an infant or child should stop breast feeding during and for 2 weeks after therapy

Initial approval duration: 6 months

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

1. Individual continues to be in consultation with an Oncologist

2. Individual's condition responded while on therapy
   - Response is defined as:
     - No evidence of disease progression
     - No evidence individual has developed any significant unacceptable adverse drug reactions that may exclude continued use
     - Dose is at least 50 mg twice daily

3. Individual has been adherent with the medication

4. Individual has not developed any significant level 4 adverse drug effects that may exclude continued use
   - Significant adverse effect such as:
     - Developed non-cutaneous RAS mutation-positive malignancy
     - Cutaneous reactions that are moderate or severe and not improving within 3 weeks despite interruption and dose reduction
     - Uveitis: mild or moderate or greater uveitis including iritis and iridocyclitis of > 6 weeks duration that did not improve with dose interruption and dose reduction
     - Developed Fever > 104^{o}F, with rigors, hypotension, dehydration, or renal failure
     - Life-threatening hemorrhage or persistent severe but not life-threatening hemorrhage that did not improve
     - Any moderate or severe reaction that does not improve after dose modification
     - Any first occurrence or recurrence of a life-threatening reaction

5. There are no significant interacting drugs

Renewal duration: 12 months

Description:

Tafinlar (dabrafenib) is indicated as a single agent for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation; it is indicated in combinations with trametinib for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K; it is indicated in combination with

trametinib, for the adjuvant treatment of patients with melanoma with BRAF V600E or V600K mutations and involvement of lymph node(s), following complete resection; it is indicated in combination with trametinib for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with BRAF V600 E mutations; and it is indicated in combination with trametinib, for the treatment of patients with locally advanced or metastatic anaplastic thyroid cancer (ATC) with BRAF V600E mutation and with no satisfactory locoregional treatment options.

Tafinlar is not indicated for treatment of patients with wild-type BRAF melanoma or wild-type BRAF NSCLC, or wild-type BRAF ATC.

Protein kinases (PKs) are a group of enzymes that modify other proteins by chemically adding a phosphate group from ATP to a target molecule, usually on the serine, threonine, or tyrosine amino acid residues. PKs can be subdivided or characterized by the amino acid that is phosphorylated: most PKs act on both serine and threonine, tyrosine kinases act on tyrosine, and a number (dual-specificity kinases) act on all three. There are PKs that phosphorylate other amino acids, such as histidine kinases that phosphorylate histidine residues. The human genome contains more than 500 PKs (the human kinome) that have a role in inflammation, autoimmunity, and metabolism.

Phosphorylation results in a functional change of the target protein which in turn changes enzyme activity, cellular location, or association with other proteins. Processes regulated by phosphorylation include ion transport, cellular proliferation, differentiation, metabolism, migration, cellular survival, and hormone responses. Phosphorylation is a necessary step in some cancers and inflammatory diseases. Inhibition of protein kinase phosphorylation is a pharmacologic target that can be used to treat these diseases.

A protein kinase inhibitor is a type of enzyme inhibitor that specifically blocks the action of one or more PKs. There are over 20 small molecule protein kinase inhibitors approved for the treatment of various conditions. Several inhibitors have been successfully used to treat human cancers; these agents have been shown to inhibit multiple cellular functions of cancer cells, including proliferation, differentiation, survival, invasion, and angiogenesis.

The BRAF human gene makes a protein called BRAF. The protein catalyzes the phosphorylation of serine and threonine residues on a target protein by use of adenosine triphosphate (ATP) conversion to adenosine diphosphate (ADP). This protein plays a role in regulating the mitogen-activated protein kinase/extracellular signal-regulated protein kinase (MAP kinase/ERKs signaling pathway), which affects cell division, differentiation, and secretion.

Acquired mutations in this gene have been found in malignant melanoma. 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; it 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.

Tafinlar is an inhibitor of some mutated forms of BRAF kinases. Some mutations in the BRAF gene, including those that result in BRAF V600E, can result in constitutively activated BRAF kinases that may stimulate tumor cell growth. Tafinlar inhibits BRAF V600 mutation-positive melanoma cell growth in vitro and in vivo.

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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:

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.

Tafinlar® package insert revised by manufacturer on 06-2017, accessed 2-27-2018.

Tafinlar® package insert revised by manufacturer on 06-2016, reviewed on 01-26-2017.

Tafinlar® package insert revised by manufacturer on 01-2014, reviewed on 02-26-2014.

Tafinlar® package insert (reference ID: 3315786) revised by manufacturer on 05-2013, reviewed on 06-13-2013.

FDA-approved tests for the detection of BRAF V600 mutations in melanoma is available at: http://www.fda.gov/CompanionDiagnositics

2009 Sept 15: US Department of Health and Human Services, National Institutes of Health, National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) Version 4.02.

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Tafinlar (dabrafenib) product information accessed 07-18-18 at DailyMed: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=fee1e6b1-e1a5-4254-9f2e-a70e0f8dbdea

NCCN Clinical Practice Guidelines in Oncology: Melanoma. Version 3.2018, July 12, 2018. https://www.nccn.org/professionals/physician_gls/pdf/melanoma.pdf

NCCN Clinical Practice Guidelines in Oncology: Non-Small Cell Lung Cancer. Version 5.2018, June 27, 2018. https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf

NCCN Clinical Practice Guidelines in Oncology: Thyroid Carcinoma. Version 1.2018, May 22, 2018. https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf

NCCN Clinical Practice Guidelines in Oncology: Central Nervous System Cancers. Version 1.2018, March 20, 2018. https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:	Dosage Form:
Directions for Use:	Quantity: / Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.