BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

TAFINLAR® (dabrafenib) oral
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** Tafinlar (dabrafenib) and/or generic equivalent (if available) are considered ***medically necessary*** and will be approved when **ALL** 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 has a confirmed diagnosis of **ONE** of the following:
    a. Single agent treatment of **unresectable or metastatic melanoma** with BRAF V600E mutation in an adult (18 years of age or older)

    b. Combination therapy with Mekinist (trametinib), for the treatment of **unresectable or metastatic melanoma** with BRAF V600E or V600K mutation in an adult (18 years of age or older)

c. Combination therapy with Mekinist (trametinib), for the adjuvant treatment of **melanoma** with BRAF V600E or V600K mutations, and with involvement of lymph node(s), following complete resection in an adult (18 years of age or older)

d. Combination therapy with Mekinist (trametinib), for the treatment of **metastatic non-small cell lung cancer (NSCLC)** with BRAF V600E mutation in an adult (18 years of age or older)

e. Combination therapy with Mekinist (trametinib), for the treatment of **locally advanced or metastatic anaplastic thyroid cancer (ATC)** with BRAF V600E mutation and with no satisfactory locoregional treatment options in an adult (18 years of age or older)

f. Combination with Mekinist (trametinib), for the treatment of adult and pediatric individuals 1 year of age or older with **unresectable or metastatic solid tumors** with BRAF V600E mutation who have progressed following prior treatment and have no satisfactory alternative treatment options

g. Combination with Mekinist (trametinib), for the treatment of pediatric individual 1 year of age or older **with low-grade glioma (LGG)** with a BRAF V600E mutation who require systemic therapy

h. 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

3. There is confirmation individual does not have wild-type BRAF solid tumors

4. There is confirmation individual does not have colorectal cancer

5. Individual has received and completed **ALL** the following **baseline tests** before initiation of treatment and with continued monitoring of the individual as clinically appropriate:
   a. An FDA-approved test confirming the presence of BRAF V600E or V600K mutation for melanoma and NSCLC. [Note: FDA-approved confirmation test for other indications is not available]
   b. Assessment of left ventricular ejection fraction by echocardiogram or multi-gated acquisition scan
   c. Serum glucose in individual with preexisting diabetes or hyperglycemia
   d. Negative pregnancy test in a woman of childbearing age
   e. Eastern Cooperative Oncology Group (ECOG) Performance Status of 0-2

6. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance, to the generic should be reported to the FDA] (see Definitions section)

7. Agent will not be used in a patient with moderate (bilirubin > 1.5x to 3x ULN and any aspartate aminotransferase (AST)) to severe (bilirubin > 3x to 10x ULN and any AST) hepatic impairment

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Tafinlar (dabrafenib) and/or generic equivalent (if available) are considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

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 with response defined as there is no evidence of disease progression or unacceptable toxicity

3. Individual has been adherent with the medication

4. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance, to the generic should be reported to the FDA] (see Definitions section)

5. Individual has not developed any significant adverse drug effects that may exclude continued use, if clinically appropriate withhold, reduce dose, or permanently discontinue based on severity, recurrence, persistence, or duration of adverse reaction as follows:
    a. Developed RAS mutation-positive non-cutaneous malignancy
    b. Uveitis: Severe uveitis including iritis and iridocyclitis does not improve with dose interruption and dose reduction
    c. Developed Fever > 104°F, with rigors, hypotension, dehydration, or renal failure
    d. Skin:
        i. Moderate or severe or life-threatening reaction that does not improve after dose modification
        ii. Severe cutaneous adverse reaction (SCARS) such as Stevens-Johnson syndrome (SJS), drug reaction with eosinophilia and systemic symptoms (DRESS)
    e. Hemophagocytic lymphohistiocytosis (HLH)
    f. Life-threatening hemorrhage or severe hemorrhage that does not improve
    g. Any moderate or severe reaction that does not improve after dose modification
    h. Any first occurrence or recurrence of a life-threatening reaction

6. Agent will not be used in a patient with moderate (bilirubin > 1.5x to 3x ULN and any aspartate aminotransferase (AST)) to severe (bilirubin > 3x to 10x ULN and any AST) hepatic impairment

Renewal duration: Up to 12 months
The recommended duration of treatment is until disease progression or unacceptable toxicity for individuals with unresectable or metastatic melanoma or solid tumors, metastatic NSCLC, or locally advanced or metastatic anaplastic thyroid cancer, or LGG

The recommended duration of treatment is until disease recurrence or unacceptable toxicity for up to 1 year in the adjuvant melanoma setting

- 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**

PHARMACY COVERAGE GUIDELINE

TAFINLAR® (dabrafenib) oral
Generic Equivalent (if available)

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 loco-regional treatment options. Tafinlar (dabrafenib) is also indicated in combination with trametinib, for the treatment of adult and pediatric patients 1 years of age and older with unresectable or metastatic solid tumors with BRAF V600E mutation who have progressed following prior treatment and have no satisfactory alternative treatment options. This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s). Tafinlar (dabrafenib) is also indicated in combination with trametinib, for the treatment of pediatric patients 1 year of age or older with low-grade glioma (LGG) with a BRAF V600E mutation who require systemic therapy.

Tafinlar is not indicated for treatment of patients with colorectal cancer because of known intrinsic resistance to BRAF inhibition. 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.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

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:

Tafinlar (dabrafenib) tab for oral susp & cap product information, revised by Novartis Pharmaceuticals Corporation 07-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed December 06, 2024.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Melanoma: Cutaneous Version 2.2025 – Updated January 28, 2025. Available at https://www.nccn.org. Accessed January 31, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Non-Small Cell Lung Cancer Version 3.2025 – Updated January 14, 2025. Available at https://www.nccn.org. Accessed January 31, 2025.

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National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Thyroid Carcinoma Version 4.2024 – Updated January 15, 2025. Available at https://www.nccn.org. Accessed January 31, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Pediatric Central Nervous System Cancers Version 2.2025 – Updated January 17, 2025. Available at https://www.nccn.org. Accessed January 31, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Central Nervous System Cancers Version 4.2024 – Updated January 21, 2025. Available at https://www.nccn.org. Accessed January 31, 2025.

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.