Tafinlar® (dabrafenib)
(Oral)

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I. Length of Authorization

Coverage is provided for six months and may be renewed (unless otherwise specified).

- Adjuvant use in melanoma may be renewed for up to 1 year of therapy.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Tafinlar 50 mg capsules: 4 capsules per day
- Tafinlar 75 mg capsules: 4 capsules per day

B. Max Units (per dose and over time) [HCPCS Unit]:

- 300 mg daily

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 18 years or older; **AND**
- Patient has not received prior therapy with BRAF and/or MEK inhibitors (e.g., vemurafenib, encorafenib, cobimetinib, binimetinib, etc.) unless otherwise specified; **AND**

Universal Criteria [1]

- Left ventricular ejection fraction (LVEF) is within normal limits prior to initiating therapy and will be assessed at regular intervals (e.g., every 3 months) during treatment; **AND**
- Patient will avoid coadministration with all of the following:
  - Strong CYP3A4 inhibitors (e.g., fluconazole, itraconazole, etc.), if therapy is unavoidable, patient will be closely monitored for adverse reactions and/or dose modifications will be implemented

- Strong CYP2C8 inhibitors (e.g., gemfibrozil, clopidogrel, etc.), if therapy is unavoidable, patient will be closely monitored for adverse reactions and/or dose modifications will be implemented; **AND**

Cutaneous Melanoma † ‡ Φ [1,7]

- Patient has BRAF V600 mutation-positive disease as detected by an FDA approved or CLIA compliant test*; **AND**
  - Used in combination with trametinib as adjuvant therapy; **AND**
    - Patient has lymph node involvement following complete resection, complete lymph node dissection (CLND), therapeutic lymph node dissection (TLND), or nodal basin ultrasound surveillance; **OR**
    - Patient has clinical satellite/in-transit metastases or local satellite/in-transit recurrence with no evidence of disease (NED) after complete excision to clear margins; **OR**
  - Used in combination with trametinib OR as a single agent if BRAF/MEK inhibitor combination therapy is contraindicated; **AND**
    - Used as initial or subsequent therapy in patients with unresectable or metastatic** disease; **OR**
    - Used as re-induction therapy for patients who experience disease control *(i.e., complete response, partial response, or stable disease)* from prior BRAF inhibitor therapy, but subsequently have disease progression/relapse >3 months after treatment discontinuation

***Metastatic disease includes stage III clinical satellite/in transit metastases or local satellite/in-transit recurrence in patients with limited resectable and unresectable disease, unresectable nodal recurrence, and disseminated (unresectable) distant metastatic disease*

Non-Small Cell Lung Cancer † ‡ [1,7]

- Patient has BRAF V600E mutation-positive disease as detected by an FDA approved or CLIA compliant test*; **AND**
- Patient has recurrent, advanced, or metastatic disease (excluding locoregional recurrence or symptomatic local disease with no evidence of disseminated disease) or mediastinal lymph node recurrence with prior radiation therapy; **AND**
- Used in combination with trametinib

Anaplastic Thyroid Cancer (ATC) † Φ [1,7]

- Patient has BRAF V600E mutation-positive disease; **AND**
- Used in combination with trametinib; **AND**
  - Patient has locally advanced disease with no satisfactory locoregional treatment options; **OR**
  - Patient has metastatic disease

Differentiated Thyroid Carcinoma (Papillary, Follicular, or Hürthle Cell) ‡ [7]

- Patient has progressive and/or symptomatic BRAF V600E mutation-positive disease; **AND**
- Patient has unresectable locoregional recurrent disease, persistent disease, or distant metastases; **AND**
- Disease is not susceptible to radioactive-iodine (RAI) therapy; **AND**
- Alternative therapies (e.g., clinical trial or systemic therapy) are not available or appropriate; **AND**
- Used as a single agent

Central Nervous System (CNS) Cancers ‡ [7]

- Patient has BRAF V600E mutation-positive disease; **AND**
    - Used in combination with trametinib; **AND**
        - Patient has pilocytic astrocytoma OR pleomorphic xanthoastrocytoma (PXA) OR ganglioglioma; **AND**
            - Used as adjuvant treatment for incomplete resection, biopsy, or surgically inaccessible location; **OR**
        - Patient has recurrent or progressive low grade glioma with prior fractionated external beam radiation therapy (EBRT); **OR**
        - Patient has recurrent anaplastic glioma or glioblastoma; **OR**
- Used for brain metastases in patients with BRAF V600E mutation-positive melanoma; **AND**
    - Used in combination with trametinib; **AND**
        - Used as primary treatment in patients with small asymptomatic brain metastases; **OR**
        - Patient has recurrent limited brain metastases; **OR**
        - Used for relapsed limited brain metastases with stable systemic disease or reasonable systemic treatment options; **OR**
        - Used for recurrent extensive brain metastases with stable systemic disease or reasonable systemic treatment options

Hepatobiliary Cancers (Gallbladder Cancer, Intra/Extra-Hepatic Cholangiocarcinoma) **‡** [7]

- Used in combination with trametinib ; **AND**
- Used as subsequent therapy for progression on or after systemic treatment for unresectable or metastatic BRAF-V600E mutation positive disease

Histiocytic Neoplasms ‡ [7]

- Used as single agent therapy; **AND**
- Patient has BRAF V600E mutation-positive disease; **AND**
- Patient has one of the following:
    - Patient relapsed/refractory or symptomatic Erdheim-Chester Disease **OR**
    - Langerhans Cell Histiocytosis (LCH) **AND**

- Patient has multisystem disease with symptomatic or impending organ dysfunction; **OR**
- Patient has pulmonary disease; **OR**
- Patient has multifocal single system bone disease not responsive to treatment with a bisphosphonate and >2 lesions; **OR**
- Patient has CNS lesions; **OR**
- Patient has relapsed or refractory disease

** If confirmed using an immunotherapy assay-http://www.fda.gov/CompanionDiagnostics*

† FDA Approved Indication(s); ‡ Compendia Approved Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: major hemorrhagic events, cardiomyopathy, uveitis, severe febrile reactions, serious dermatological reactions (e.g., Stevens-Johnson syndrome [SJS] and drug reaction with eosinophilia and systemic symptoms [DRESS], etc.), hyperglycemia, new primary malignancies, hemolytic anemia in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency, etc.; **AND**
- Left ventricular ejection fraction (LVEF) has not had an absolute decrease of > 20% from baseline and is not below the lower limit of normal (LLN) *(LVEF results must be within the previous 3 months)*; **AND**

Adjuvant treatment of Melanoma

- Treatment has not exceeded 1 year of therapy

Cutaneous Melanoma (re-induction therapy) [7]

- *Refer to Section III for criteria (see Cutaneous Melanoma – Used as re-induction therapy)*

V. Dosage/Administration [1]

Indication	Dose
All indications	Administer 150 mg orally twice daily, until disease progression/recurrence or unacceptable toxicity *(Note: for adjuvant treatment of melanoma, treat until disease recurrence or unacceptable toxicity for up to 1 year).*

VI. Billing Code/Availability Information

HCPCS Code:

- J8999 – Prescription drug oral, chemotherapeutic, Not Otherwise Specified
- C9399 – Unclassified drugs or biologics (Hospital Outpatient Use Only)

NDC(s):

- Tafinlar 50 mg capsule: 00078-0682-xx
- Tafinlar 75 mg capsule: 00078-0681-xx

VII. References

1. Tafinlar [package insert]. East Hanover, NJ; Novartis Pharmaceuticals Corporation; April 2020. Accessed September 2020.
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3. Hauschild A, Grob JJ, Demidov LV, et al. Dabrafenib in BRAF-mutated metastatic melanoma: a multicentre, open-label, phase 3 randomised controlled trial. Lancet. 2012 Jul 28; 380(9839):358-65.
4. Long GV, Trefzer U, Davies MA, et al. Dabrafenib in patients with Val600Glu or Val600Lys BRAF-mutant melanoma metastatic to the brain (BREAK-MB): a multicentre, open-label, phase 2 trial. Lancet Oncol. 2012 Nov; 13(11):1087-95.
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7. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) dabrafenib. National Comprehensive Cancer Network, 2020. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed September 2020.
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10. Long GV, Hauschild A, Santinami M, et al. Adjuvant Dabrafenib plus Trametinib in Stage III BRAF-Mutated Melanoma. N Engl J Med 2017; 377:1813-1823.
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Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C22.1	Intrahepatic bile duct carcinoma
C23	Malignant neoplasm of gallbladder
C24.0	Malignant neoplasm of extrahepatic bile duct
C24.8	Malignant neoplasm of overlapping sites of biliary tract
C24.9	Malignant neoplasm of biliary tract, unspecified
C33	Malignant neoplasm of trachea
C34.00	Malignant neoplasm of unspecified main bronchus
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus
C34.10	Malignant neoplasm of upper lobe, unspecified bronchus or lung
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.30	Malignant neoplasm of lower lobe, unspecified bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.80	Malignant neoplasm of overlapping sites of unspecified bronchus or lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung
C34.90	Malignant neoplasm of unspecified part of unspecified bronchus or lung
C34.91	Malignant neoplasm of unspecified part of right bronchus or lung
C34.92	Malignant neoplasm of unspecified part of left bronchus or lung
C43.0	Malignant melanoma of lip

ICD-10	ICD-10 Description
C43.10	Malignant melanoma of unspecified eyelid, including canthus
C43.111	Malignant melanoma of right upper eyelid, including canthus
C43.112	Malignant melanoma of left lower eyelid, including canthus
C43.121	Malignant melanoma of left upper eyelid, including canthus
C43.122	Malignant melanoma of left lower eyelid, including canthus
C43.20	Malignant melanoma of unspecified ear and external auricular canal
C43.21	Malignant melanoma of right ear and external auricular canal
C43.22	Malignant melanoma of left ear and external auricular canal
C43.30	Malignant melanoma of unspecified part of face
C43.31	Malignant melanoma of nose
C43.39	Malignant melanoma of other parts of face
C43.4	Malignant melanoma of scalp and neck
C43.51	Malignant melanoma of anal skin
C43.52	Malignant melanoma of skin of breast
C43.59	Malignant melanoma of other part of trunk
C43.60	Malignant melanoma of unspecified upper limb, including shoulder
C43.61	Malignant melanoma of right upper limb, including shoulder
C43.62	Malignant melanoma of left upper limb, including shoulder
C43.70	Malignant melanoma of unspecified lower limb, including hip
C43.71	Malignant melanoma of right lower limb, including hip
C43.72	Malignant melanoma of left lower limb, including hip
C43.8	Malignant melanoma of overlapping sites of skin
C43.9	Malignant melanoma of skin, unspecified
C71.1	Malignant neoplasm of frontal lobe
C71.2	Malignant neoplasm of temporal lobe
C71.3	Malignant neoplasm of parietal lobe
C71.4	Malignant neoplasm of occipital lobe
C71.5	Malignant neoplasm of cerebral ventricle
C71.6	Malignant neoplasm of cerebellum
C71.7	Malignant neoplasm of brain stem
C71.8	Malignant neoplasm of overlapping sites of brain
C71.9	Malignant neoplasm of brain, unspecified
C72.0	Malignant neoplasm of spinal cord
C72.9	Malignant neoplasm of central nervous system, unspecified

ICD-10	ICD-10 Description
C73	Malignant neoplasm of thyroid gland
C96.0	Multifocal and multisystemic (disseminated) Langerhans-cell histiocytosis
C96.20	Malignant mast cell neoplasm unspecified
C96.5	Multifocal and unisystemic Langerhans-cell histiocytosis
C96.6	Unifocal Langerhans-cell histiocytosis
C96.9	Malignant neoplasm of lymphoid, hematopoietic and related tissue, unspecified
C96.Z	Other specified malignant neoplasms of lymphoid, hematopoietic and related tissue
D43.0	Neoplasm of uncertain behavior of brain, supratentorial
D43.1	Neoplasm of uncertain behavior of brain, infratentorial
D43.2	Neoplasm of uncertain behavior of brain, unspecified
D43.4	Neoplasm of uncertain behavior of spinal cord
D43.9	Neoplasm of uncertain behavior of central nervous system, unspecified
D76.3	Other histiocytosis syndromes
C79.31	Secondary malignant neoplasm of brain
Z85.118	Personal history of other malignant neoplasm of bronchus and lung
Z85.820	Personal history of malignant melanoma of skin
Z85.841	Personal history of malignant neoplasm of brain

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC