PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Tafinlar Prior Authorization Policy
- Tafinlar® (dabrafenib capsules and tablets for oral suspension – Novartis)

REVIEW DATE: 04/05/2023; selected revision 09/13/2023

INSTRUCTIONS FOR USE

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CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Tafinlar, a BRAF inhibitor, is indicated for the following uses:[1]

- **Low-grade glioma,** in combination with Mekinist, for the treatment of pediatric patients ≥ 1 year of age with a BRAF V600E mutation who require systemic therapy.
- **Melanoma**, in the following situations:[1]
  - As a single agent for unresectable or metastatic disease with *BRAF V600E* mutation as detected by an FDA-approved test.
  - In combination with Mekinist® (trametinib tablets and oral solution), for unresectable or metastatic disease with a *BRAF V600E* or *V600K* mutation, as detected by an FDA-approved test.
  - In combination with Mekinist, as adjuvant treatment of *BRAF V600E* or *V600K* mutation-positive disease as detected by an FDA-approved test, with involvement of the lymph node(s), following complete resection.
- **Non-small cell lung cancer**, in combination with Mekinist for disease that has the *BRAF V600E* mutation as detected by an FDA-approved test.
- **Solid tumors - unresectable or metastatic**, in combination with Mekinist, for *BRAF V600E* mutation-positive disease, as determined by an FDA-approved test, in patients ≥ 1 year of age who have no satisfactory alternative treatment options.

- **Thyroid cancer**, in combination with Mekinist, for locally advanced or metastatic anaplastic disease with *BRAF V600E* mutation and with no satisfactory locoregional treatment options.

Limitations of Use**:** Tafinlar is not indicated for treatment of patients with colorectal cancer because of the known intrinsic resistance to BRAF inhibition. Tafinlar is not indicated for treatment of patients with wild-type BRAF solid tumors.

Dosing: For the tablet dosage form, Tafinlar has dosing for patients who are adults and for patients who are between 6 and 17 years of age and weigh ≥ 26 kg. The oral solution dosage form also has weight-based dosing for patients ≥ 8 kg.

Guidelines

National Comprehensive Cancer Network (NCCN) guidelines support use in multiple cancers.

- **Central Nervous System Cancers:** Guidelines (version 1.2023 – March 24, 2023) recommend a BRAF/MEK inhibitor combination (i.e., Tafinlar/Mekinist or Zelboraf® [vemurafenib tablets]/Cotellic® [cobimetinib tablets]) for treatment of *BRAF V600E* activation mutations in adults in the following situations: adjuvant treatment of pilocytic astrocytoma, pleomorphic xanthoastrocytoma, or ganglioglioma; recurrent or progressive low-grade glioma, oligodenroglioma, or isocitrate dehydrogenase-2 (*IDH2*)-mutant astrocytoma; and recurrent glioblastoma. BRAF/MEK combination therapy is also recommended for melanoma with brain metastases.[6] Guidelines for pediatric central nervous system (CNS) cancers (version 2.2023 – October 31, 2022) include targeted therapy with Tafinlar + Mekinist as adjuvant therapy or for recurrent or progressive disease if the cancer has a *BRAF V600E* mutation.[9]
- **Histiocytic Neoplasms:** Guidelines (version 1.2022 – May 20, 2022) recommend Zelboraf as "preferred" or Tafinlar as "other recommended regimen" for *BRAF V600E*-mutated Erdheim-Chester disease, and for multisystem, pulmonary, or CNS Langerhans cell histiocytosis.[5]
- **Melanoma, Cutaneous:** Guidelines (version 2.2023 – March 10, 2023) recommend BRAF/MEK inhibitor combinations among the preferred therapies for first-line and subsequent treatment of metastatic or unresectable melanoma with a *V600*-activating mutation.[2] While combination BRAF/MEK inhibition is preferred, if a combination is contraindicated, monotherapy with a BRAF inhibitor is an option. Tafinlar + Mekinist is also recommended in guidelines as adjuvant therapy (including for nodal recurrence) in some patients with Stage III disease, including use post-surgery or use after complete lymph node dissection. If unacceptable toxicity to Tafinlar/Mekinist, other BRAF/MEK combinations can be considered.
- **Non-Small Cell Lung Cancer:** Guidelines (version 2.2023 – February 17, 2023) list Tafinlar + Mekinist among the first-line therapy and subsequent therapy options for tumors with a *BRAF* mutation.[3] NCCN also notes that monotherapy with a BRAF inhibitor (Tafinlar or Zelboraf) is a treatment option when combination therapy is not tolerated.

The NCCN Compendium[7] recommends use of Tafinlar, in combination with Mekinist, for the following *BRAF V600* positive tumors (all category 2A): High-grade gliomas, ampullary adenocarcinoma, neuroendocrine tumors, pancreatic adenocarcinoma, salivary gland tumors, ovarian/fallopian tube/primary peritoneal cancer, esophageal and esophagogastric junction cancers, gastric cancer, biliary tract cancers, gastrointestinal stromal tumors, brain metastases due to melanoma, and differentiated thyroid carcinoma.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Tafinlar. All approvals are provided for the duration noted below.

- **Tafinlar® (dabrafenib capsules and tablets for oral suspension (Novartis)**

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indications

1. **Low Grade Glioma.** Approve for 1 year if the patient meets the following (A, B, C, and D):
   A) Patient is ≥ 1 year of age; AND
   B) Patient has *BRAF V600* mutation-positive disease; AND
   C) The medication will be taken in combination with Mekinist (trametinib tablets or oral solution); AND
   D) Patient requires systemic therapy.

2. **Melanoma.** Approve for 1 year if the patient meets the following (A, B, and C):
   A) Patient is ≥ 6 years of age; AND
   B) Patient has unresectable, advanced (including Stage III or Stage IV disease), or metastatic melanoma; AND
   Note: This includes adjuvant treatment in patients with Stage III disease with no evidence of disease post-surgery.
   C) Patient has *BRAF V600* mutation-positive disease.

3. **Non-Small Cell Lung Cancer.** Approve for 1 year if the patient meets the following (A and B)
   A) Patient is ≥ 6 years of age; AND
   B) Patient has *BRAF V600* mutation-positive disease.

4. **Solid Tumors – Unresectable or Metastatic.** Approve for 1 year if the patient meets the following (A, B, C, and D):
   Note: Examples of solid tumors are: biliary tract cancer, brain metastases due to melanoma, high-grade gliomas, ovarian/fallopian tube/primary peritoneal cancer, differentiated thyroid carcinoma, gastrointestinal stromal tumors, gastric cancer,

esophageal and esophagogastric junction cancers, salivary gland tumors, pancreatic adenocarcinoma, neuroendocrine tumors, and ampullary adenocarcinoma.
A) Patient is ≥ 1 year of age; AND
B) Patient has *BRAF V600* mutation-positive disease; AND
C) The medication will be taken in combination with Mekinist (trametinib tablets or oral solution); AND
D) According to the prescriber, the patient has no satisfactory alternative treatment options.

5. **Thyroid Carcinoma, Anaplastic.** Approve for 1 year if the patient meets the following (A, B, C, and D):
A) Patient is ≥ 6 years of age; AND
B) Patient has locally advanced or metastatic anaplastic disease; AND
C) Patient has *BRAF V600* mutation-positive disease; AND
D) The medication will be taken in combination with Mekinist (trametinib tablets or oral solution), unless intolerant.

Other Uses with Supportive Evidence

6. **Histiocytic Neoplasm.** Approve for 1 year if the patient meets the following (A, B, and C):
A) Patient is ≥ 6 years of age; AND
B) Patient meets one of the following (i or ii):
i. Patient has Langerhans cell histiocytosis AND one of the following (a, b, or c):
a) Multisystem disease; OR
b) Pulmonary disease; OR
c) Central nervous system lesions; OR
ii. Patient has Erdheim-Chester disease; AND
C) Patient has *BRAF V600*-mutation positive disease.

CONDITIONS NOT COVERED

- **Tafinlar® (dabrafenib capsules and tablets for oral suspension (Novartis)**

is(are) considered experimental, investigational or unproven for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Colon or Rectal Cancer.** Tafinlar is not indicated for treatment of patients with colorectal cancer because of known intrinsic resistance to BRAF inhibition.[1]

REFERENCES

1. Tafinlar® capsules and tablets for oral suspension [prescribing information]. East Hanover, NJ: Novartis; August 2023.

2. The NCCN Melanoma: Cutaneous Clinical Practice Guidelines in Oncology (version 2.2023 – March 10, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org/. Accessed on April 3, 2023.
3. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (version 2.2023 – February 17, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org/. Accessed on April 3, 2023.
4. The NCCN Thyroid Carcinoma Clinical Practice Guidelines in Oncology (version 1.2023 – March 24, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org/. Accessed on April 3, 2023.
5. The NCCN Histiocytic Neoplasms Clinical Practice Guidelines in Oncology (version 1.2022 – May 20, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org/. Accessed on April 3, 2023.
6. The NCCN Central Nervous System Cancers Clinical Practice Guidelines in Oncology (version 1.2023 – March 24, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org/. Accessed on April 3, 2023.
7. The NCCN Drugs & Biologics Compendium. © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 3, 2023. Search term: dabrafenib.

HISTORY

Type of Revision	Summary of Changes	Review Date
Selected Revision	Approval durations were changed from 3 years to 1 year.	06/22/2022
Annual Revision	**Melanoma:** The required age was changed from ≥ 18 years of age to be ≥ 6 years of age. A requirement was added that the patient weighs ≥ 26 kg. **Metastatic or Solid Tumors:** This newly approved condition was added to the policy. **Non-Small Cell Lung Cancer:** The required age was changed from ≥ 18 years of age to be ≥ 6 years of age. A requirement was added that the patient weighs ≥ 26 kg. **Thyroid Cancer, Anaplastic:** The required age was changed from ≥ 18 years of age to be ≥ 6 years of age. A requirement was added that the patient weighs ≥ 26 kg. **Biliary Tract Cancer:** The required age was changed from ≥ 18 years of age to be ≥ 6 years of age. A requirement was added that the patient weighs ≥ 26 kg. **Central Nervous System Cancer:** The required age was changed from ≥ 18 years of age to be ≥ 6 years of age. A requirement was added that the patient weighs ≥ 26 kg. To align with guidelines, criteria for recurrent disease now also apply for progressive disease. For a patient with glioma, the qualifier of "low grade" was removed. To align with guidelines, anaplastic glioma was removed and replaced with isocitrate dehydrogenase-2-mutant astrocytoma or oligodendroglioma. **Histiocytic Neoplasm:** The required age was changed from ≥ 18 years of age to be ≥ 6 years of age. A requirement was added that the patient weighs ≥ 26 kg. **Ovarian, Fallopian Tube, or Primary Peritoneal Cancer:** To align with guidelines, this condition was added to the policy. **Thyroid Cancer, Differentiated:** The required age was changed from ≥ 18 years of age to be ≥ 6 years of age. A requirement was added that the patient weighs ≥ 26 kg. **Conditions Not Covered:** Colon or Rectal Cancer was added to this section of the policy.	08/03/2022

Early Annual Revision	Added new oral solution formulation to the policy. For all indications, removed weight ≥ 26 kg criterion due to the approval of an oral suspension formulation for ≥ 8 kg. **Solid Tumors – Unresectable or Metastatic:** Modified indication to match FDA label. Previously listed as "Metastatic or solid tumors." Included "Note" below indication heading with a long list of examples of solid tumors that are supported by National Comprehensive Cancer Network (NCCN) guidelines/compendium. For criterion D, added phrase "According to the prescriber" in reference to unavailability of satisfactory alternative treatment options. **Non-Small Cell Lung Cancer:** Similar to other criteria, deleted "E" from *BRAF V600* mutation reference. This is due to the possibility of occurrence of other point mutations than V600E. **Low Grade Glioma:** Added new condition and criteria based on FDA-approval **Other Uses with Supportive Evidence:** Deleted Biliary Tract Cancer, Central Nervous System Cancer, Ovarian, Fallopian Tube, or Primary Peritoneal Cancer, and Thyroid Cancer, Differentiated conditions since they are now listed as examples under FDA-approved use "Solid Tumors – Unresectable or Metastatic." Histiocytic Neoplasm was not deleted because combination use with Mekinist is not required for this condition (Solid Tumor indication requires use with Mekinist).	04/05/2023
Selected Revision	**Solid Tumors – Unresectable or Metastatic:** Age indication expanded for use in patients 1 year and older. The required age was changed from ≥ 6 years of age to be ≥ 1 years of age.	09/13/2023

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