



PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Tafinlar® (dabrafenib capsules – GlaxoSmithKline)

TAC APPROVAL DATE: 06/18/2019

OVERVIEW

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

1. Melanoma, in the following situations:
 - as a single agent for the treatment of patients with unresectable or metastatic disease with *BRAF V600E* mutation as detected by an FDA-approved test;¹ AND
 - in combination with Mekinist® (trametinib tablets), for the treatment of patients with unresectable or metastatic disease with *BRAF V600E* or *V600K* mutations as detected by an FDA-approved test; AND
 - as adjuvant treatment of *BRAF V600E* or *V600K* mutation-positive disease as detected by an FDA-approved test, and involvement of the lymph node(s), following complete resection; AND
2. Non-small cell lung cancer (NSCLC), in combination with Mekinist for treatment of disease that has the *BRAF V600E* mutation as detected by an FDA-approved test; AND
3. Thyroid cancer, in combination with Mekinist, for treatment of patients with locally advanced or metastatic anaplastic disease with *BRAF V600E* mutation and with no satisfactory locoregional treatment options.

Tafinlar is not indicated for the treatment of patients with wild-type BRAF disease.

Disease Overview

Mutations in the BRAF gene are common in several types of cancer.² The BRAF protein is normally switched on and off in response to signals that control cell growth and development; however, mutations cause the BRAF protein to be continuously active. This over activity may contribute to the growth of cancers by allowing abnormal cells to grow and divide uncontrollably. The V600E mutation is the most common *BRAF* gene mutation identified in cancers, particularly in melanoma.

Guidelines

The National Comprehensive Cancer Network (NCCN) supports use of Mekinist in multiple cancers.

FDA-Approved Indications

- Melanoma: Guidelines (version 2.2019 – March 12, 2019) recommend BRAF + MEK inhibitor combinations (e.g., Zelboraf + Cotellic, Tafinlar + Mekinist, Braftovi + Mektovi) for first-line (preferred if clinically needed for early response) and subsequent treatment of metastatic or unresectable melanoma with a V600 activating mutation.³ While combination BRAF/MEK inhibition is preferred, NCCN notes that if contraindicated, monotherapy with a BRAF inhibitor (Tafinlar or Zelboraf) are recommended options, particularly for patients who are not appropriate candidates for checkpoint immunotherapy. 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.

- Non-Small Cell Lung Cancer (NSCLC): Guidelines (version 4.2019 – April 29, 2019) list Tafinlar + Mekinist as a first-line therapy for tumors with a *BRAF* mutation.⁴ NCCN also notes that monotherapy with a BRAF inhibitor (Tafinlar or Zelboraf) is a treatment option when combination therapy is not tolerated.
- Thyroid Cancer: Guidelines (version 1.2019 – May 28, 2019) list Tafinlar + Mekinist as a treatment option for metastatic anaplastic thyroid cancer with a *BRAF* mutation.⁵

Other Uses With Supportive Evidence

- Colon Cancer: Guidelines (version 2.2019 – May 15, 2019) recommend BRAF/MEK inhibitor combinations for *BRAF V600E*-mutated disease.⁴ For primary treatment (following adjuvant chemotherapy) or as subsequent use, Zelboraf + irinotecan + Erbitux (cetuximab IV infusion) or Vectibix (panitumumab IV infusion) is a recommended treatment option. Subsequent use of either Braftovi + Mektovi or Tafinlar + Mekinist are also treatment options recommended in combination with Erbitux or Vectibix.
- Thyroid Cancer: Tafinlar and Zelboraf are also treatment options for the treatment of iodine-refractory differentiated thyroid cancer with a *BRAF V600E* mutation. This recommendation is for follicular, Hürthle cell, and papillary cancer subtypes.

POLICY STATEMENT

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

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Tafinlar is recommended in those who meet the following criteria:

FDA-Approved Indications

- 1. Melanoma.** Approve for 3 years if the patient meets BOTH of the following (A and B):
 - A) The patient has unresectable, advanced (including Stage III or Stage IV disease), or metastatic melanoma. NOTE: This includes adjuvant treatment in patients with Stage III disease with no evidence of disease post-surgery; AND
 - B) The patient has *BRAF V600* mutation-positive disease.
- 2. Non-Small Cell Lung Cancer (NSCLC).** Approve for 3 years if the patient has *BRAF V600E* mutation-positive disease.
- 3. Thyroid Cancer, Anaplastic.** Approve for 3 years if the patient meets ALL of the following (A, B, and C):
 - A) The patient has locally advanced or metastatic anaplastic disease; AND
 - B) Tafinlar will be taken in combination with Mekinist, unless intolerant; AND
 - C) The patient has *BRAF V600* mutation-positive disease.

Other Uses with Supportive Evidence

- 4. Colon or Rectal Cancer.** Approve for 3 years if the patient meets the following (A, B, and C):
 - A) The patient has *BRAF V600E* mutation-positive disease; AND

- B) The patient has previously received a chemotherapy regimen for colon or rectal cancer. NOTE: examples of chemotherapy regimens include a fluoropyrimidine such as 5-fluorouracil (5-FU), capecitabine; oxaliplatin, irinotecan, or an adjunctive chemotherapy regimen such as FOLFOX (5-FU, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin); AND
- C) The agent is prescribed as part of a combination regimen for colon or rectal cancer. NOTE: examples of combination regimens include: Tafinlar/Mekinist (trametinib tablets)/Erbix (cetuximab IV infusion), Tafinlar/Mekinist/Vectibix (panitumumab IV infusion).

5. Thyroid Cancer, Differentiated. Approve for 3 years if the patient meets ALL of the following conditions (A, B, and C):

- A) The patient has differentiated thyroid carcinoma. NOTE: This includes papillary, follicular, or Hürthle cell differentiated thyroid cancer; AND
- B) The patient has disease that is refractory to radioactive iodine therapy; AND
- C) The patient has *BRAF* mutation-positive disease.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Tafinlar has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

- 1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Tafinlar® capsules [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; May 2018.
2. Genetic Home Reference. BRAF gene. National Institutes of Health, US Department of Health & Human Service Web Site. Reviewed August 2018. Accessed on June 4, 2019. Available at: <https://ghr.nlm.nih.gov/gene/BRAF>.
3. The NCCN Melanoma Clinical Practice Guidelines in Oncology (Version 2.2019 – March 12, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on June 4, 2019.
4. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (Version 4.2019 – April 29, 2019). © 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on June 6, 2019.
5. The NCCN Thyroid Carcinoma Clinical Practice Guidelines in Oncology (Version 1.2019 – May 28, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on June 6, 2019.

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
Annual revision	For melanoma, modify criteria for use as monotherapy to only include patients who have <u>not</u> previously experienced disease progression on prior BRAF inhibitor treatment. Previously, this was addressed in as a Condition Not Recommended for Coverage but is now being moved to the criteria section of the policy.	09/20/2017
Selected revision	Adjust melanoma criteria to remove “unresectable or metastatic” as a qualifier for melanoma and move to criteria section for initial therapy; add that “advanced” melanoma may be included in this criterion. Add a note indicating that adjuvant treatment in patients with Stage III disease with no evidence of disease post-surgery would be included in this criterion.	12/06/2017
Early annual revision	Add criteria to approve for 3 years for locally advanced or metastatic anaplastic thyroid cancer that is BRAF V600-positive, if taken in combination with Mekinist (unless intolerant). Due to new indication as adjuvant therapy in resectable melanoma, remove	05/23/2018

	criteria that does not allow coverage in patients who had disease progression while on a BRAF inhibitor. Remove continuation criteria in melanoma; now all approvals require that the patient has unresectable, advanced (including Stage III or Stage IV disease), or metastatic melanoma with a BRAF mutation. In Other Uses with Supportive Evidence, add criteria to approve for 3 years for differentiated thyroid cancer, if BRAF-positive and refractory to radioactive iodine therapy.	
Annual revision	<p>NSCLC: The diagnosis was changed to remove the BRAF mutation from the approval condition. The requirement that the patient has BRAF V600E mutation was added to the criteria for patients with NSCLC.</p> <p>Colon or Rectal Cancer: Add criteria as supported by NCCN colon cancer guidelines. Criteria approve if the patient has <i>BRAF V600E</i> mutation-positive disease, and if the patient has previously used chemotherapy, and if the agent will be used as part of a combination regimen for colon or rectal cancer.</p>	06/18/2019

*For a further summary of criteria changes, refer to respective TAC minutes available at: <http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx>. TAC – Therapeutic Assessment Committee; DEU – Drug Evaluation Unit; NCCN – National Comprehensive Cancer Network; NA – Not applicable; NSCLC – Non-small cell lung cancer.