

PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Mekinist™ (trametinib tablets – GlaxoSmithKline)

TAC APPROVAL DATE: 06/18/2019

OVERVIEW

Mekinist, a kinase inhibitor, is indicated for the treatment of patients with the following conditions:

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

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. Of note, NCCN states that two trials have demonstrated that complete lymph node dissection has no impact on disease-specific survival or overall survival; therefore, it is unclear if complete lymph node dissection should be a factor in the decision to use as adjuvant therapy

in sentinel node-positive patients. NCCN guidelines for uveal melanoma (version 1.2018 – March 15, 2018) list Mekinist as a treatment option for metastatic or unresectable disease.

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

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 Tafenlar + Mekinist are also treatment options recommended in combination with Erbitux or Vectibix.

POLICY STATEMENT

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

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Mekinist 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.** Approve for 3 years if the patient meets BOTH of the following (A and B):
 - A)** The patient has *BRAF V600E* mutation-positive disease; AND
 - B)** The agent is being used in combination with Tafenlar (dabrafenib capsules).
- 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) Mekinist will be taken in combination with Tafinlar, unless intolerant; AND
- C) The patient has *BRAF V600* mutation-positive disease.

Other Uses with Supportive Evidence

2. **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 (dabrafenib capsules)/Mekinist/Erbitux (cetuximab IV infusion), Tafinlar/Mekinist/Vectibix (panitumumab IV infusion).

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Mekinist 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. Rationale for non-coverage for these specific conditions is provided below. (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. Mekinist® tablets [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; May 2018.
2. Genetic Home Reference. BRAF gene. National Institutes of Health, US Department of Health & Human Services 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. 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.
4. Cotellic® tablets [prescribing information]. South San Francisco, CA: Genentech/Roche; January 2018.
5. The NCCN Uveal Melanoma Clinical Practice Guidelines in Oncology (Version 1.2018 – March 15, 2018). © 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on June 6, 2018.
6. 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..
7. The NCCN Colon Cancer Clinical Practice Guidelines in Oncology (Version 2.2019 – May 15, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on June 13, 2019.

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
Annual revision	Move NSCLC to an FDA-approved indication with no changes to the criteria. Remove Combination use with Zelboraf, unless already started on Mekinist from the Conditions not Recommended for Coverage (already addressed in criterion 1A and 1B). Remove use of Mekinist as a single agent in patients who have experienced disease progression on a BRAF inhibitor for melanoma (unless already started on Mekinist) from the Conditions not Recommended for Coverage (already addressed in criterion 1Aiiib).	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 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.	05/23/2018
Annual revision	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. 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.	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.