PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Mekinist Prior Authorization Policy
- Mekinist® (trametinib tablets – GlaxoSmithKline)

REVIEW DATE: 08/03/2022

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.
  - In combination with Tafinlar® (dabrafenib tablets), for unresectable or metastatic disease with a *BRAF V600E* or *V600K* mutation as detected by an FDA-approved test.
  - In combination with Tafinlar, as adjuvant treatment of *BRAF V600E* or *V600K* mutation-positive disease as detected by an FDA-approved test, with involvement of lymph nodes, following complete resection.
- **Metastatic or solid tumors**, in combination with Taflinar, for *BRAF V600E* mutation-positive disease, as determined by an FDA-approved test, in patients ≥ 6 years of age who have no satisfactory alternative treatment options.
- **Non-small cell lung cancer**, in combination with Tafinlar, for disease that has the *BRAF V600E* mutation as detected by an FDA-approved test.
- **Thyroid cancer**, in combination with Tafinlar, for locally advanced or metastatic anaplastic disease with *BRAF V600E* mutation and with no satisfactory locoregional treatment options.

For the approved indications, Mekinist has dosing for patients who are adults and for patients who are between 6 and 17 years of age and weigh ≥ 26 kg. Mekinist is not indicated for treatment of patients with colorectal cancer because of the known intrinsic resistance to BRAF inhibition.

Guidelines

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

- **Central Nervous System Cancers**: Guidelines (version 1.2022 – June 2, 2022) 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, oliogdenroglioma, or isocitrate dehydrogenase-2 (*IDH2*)-mutant astrocytoma; and recurrent glioblastoma.[7] BRAF/MEK combination therapy is also recommended for melanoma with brain metastases. Guidelines for pediatric central nervous system (CNS) cancers (version 1.2023 – July 12, 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]
- **Hepatobiliary Cancers:** Guidelines (version 2.2022 – July 15, 2022) recommend Tafinlar + Mekinist for subsequent therapy for biliary tract cancers, if the patient has a *BRAF V600E* mutation.[8]
- **Histiocytic Neoplasms:** Guidelines (version 1.2022 – May 20, 2022) recommend Cotellic (preferred) or Mekinist (other recommended regimen) for histiocytic neoplasms (if there is a MAP kinase pathway mutation, or no detectable mutation, or testing is not available) for the

following types: Langerhans cell histocytosis (including multisystem, pulmonary or central nervous system lesions), Erdheim-Chester disease, and Rosai-Dorfman disease.[6]

- **Melanoma, Cutaneous:** Guidelines for cutaneous disease (version 3.2022 – April 11, 2022) 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 3.2022 – March 16, 2022) 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.
- **Ovarian Cancer, Including Fallopian Tube and Primary Peritoneal:** Guidelines (version 2.2022 – July 13, 2022) recommend Tafinlar + Mekinist in various situations for recurrent carcinoma with a *BRAF V600E* mutation. Monotherapy with Mekinist is also among the targeted therapy options for recurrent low-grade serous disease.[5]
- **Thyroid Cancer:** Guidelines (version 2.2022 – May 5, 2022) list Tafinlar + Mekinist as a treatment option for metastatic anaplastic thyroid cancer with a *BRAF* mutation.[4]

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 one of the following criteria:

FDA-Approved Indications

1. **Melanoma.** Approve for 1 year if the patient meets the following (A, B, and C):
   - **A)** Patient meets both of the following (i and ii):
     - **i.** Patient is ≥ 6 years of age; AND
     - **ii.** Patient weighs ≥ 26 kg; 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.

2. **Metastatic or Solid Tumors.** Approve for 1 year if the patient meets the following (A, B, C, and D):
   - **A)** Patient meets both of the following (i and ii):
     - **i.** Patient is ≥ 6 years of age; AND
     - **ii.** Patient weighs ≥ 26 kg; AND
   - **B)** Patient has *BRAF V600* mutation-positive disease; AND
   - **C)** The medication will be taken in combination with Tafinlar (dabrafenib capsules); AND

D) Patient has no satisfactory alternative treatment options.

2. Non-Small Cell Lung Cancer. Approve for 1 year if the patient meets the following (A, B, and C):
- **A)** Patient meets both of the following (i and ii):
  - **i.** Patient is ≥ 6 years of age; AND
  - **ii.** Patient weighs ≥ 26 kg; AND
- **B)** Patient has *BRAF V600E* mutation-positive disease; AND
- **C)** The medication is prescribed in combination with Tafinlar (dabrafenib capsules).

3. Thyroid Carcinoma, Anaplastic. Approve for 1 year if the patient meets the following (A, B, C, and D):
- **A)** Patient meets both of the following (i and ii):
  - **i.** Patient is ≥ 6 years of age; AND
  - **ii.** Patient weighs ≥ 26 kg; AND
- **B)** Patient has locally advanced or metastatic anaplastic disease; AND
- **C)** Patient has *BRAF V600* mutation-positive disease; AND
- **D)** The medication is prescribed in combination with Tafinlar (dabrafenib capsules), unless intolerant.

Other Uses with Supportive Evidence

4. Biliary Tract Cancer. Approve for 1 year if the patient meets the following (A, B, C, and D):
- **A)** Patient meets both of the following (i and ii):
  - **i.** Patient is ≥ 6 years of age; AND
  - **ii.** Patient weighs ≥ 26 kg; AND
- **B)** Patient has tried at least one systemic chemotherapy regimen; AND
- **C)** Patient has *BRAF V600* mutation-positive disease; AND
- **D)** The medication is prescribed in combination with Tafinlar (dabrafenib capsules).

5. Central Nervous System Cancer. Approve for 1 year if the patient meets the following (A, B, C, and D):
- **A)** Patient meets both of the following (i and ii):
  - **i.** Patient is ≥ 6 years of age; AND
  - **ii.** Patient weighs ≥ 26 kg; AND
- **B)** The medication is being used for one of the following situations (i, ii, or iii):
  - **i.** Adjuvant treatment of one of the following conditions (a, b, or c):
    - **a)** Pilocytic astrocytoma; OR
    - **b)** Pleomorphic xanthoastrocytoma; OR
    - **c)** Ganglioglioma; OR
  - **ii.** Recurrent or progressive disease for one of the following conditions (a, b, c, or d):
    - **a)** Glioma; OR
    - **b)** Isocitrate dehydrogenase-2 (IDH2)-mutant astrocytoma; OR
    - **c)** Oligodendroglioma; OR
    - **d)** Glioblastoma; OR
  - **iii.** Brain metastases from melanoma; AND
- **C)** Patient has *BRAF V600* mutation-positive disease; AND
- **D)** The medication is prescribed in combination with Tafinlar (dabrafenib capsules).

6. Histiocytic Neoplasm. Approve for 1 year if the patient meets the following (A and B):
- **A)** Patient meets both of the following (i and ii):
  - **i.** Patient is ≥ 6 years of age; AND

ii. Patient weighs ≥ 26 kg; AND

B) Patient meets one of the following (i, ii, or iii):

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; OR

iii. Patient has Rosai-Dorfman disease.

7. Ovarian, Fallopian Tube, or Primary Peritoneal Cancer. Approve for 1 year if the patient meets the following (A, B, and C):

A) Patient meets both of the following (i and ii):

i. Patient is ≥ 6 years of age; AND

ii. Patient weighs ≥ 26 kg; AND

B) Patient has recurrent disease; AND

C) Patient meets ONE of the following (i or ii):

i. The medication is used for low-grade serous carcinoma; OR

ii. The patient meets both of the following (a and b):

a) Patient has *BRAF V600* mutation-positive disease; AND

b) The medication will be taken in combination with Tafinlar (dabrafenib capsules).

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Mekinist is not recommended in the following situations:

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

2. 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; June 2022.
2. The NCCN Melanoma Clinical Practice Guidelines in Oncology (version 3.2022 – April 11, 202221). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org/. Accessed on July 24, 2022.
3. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (version 2.2022 – March 16, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org/. Accessed on July 25, 2022.
4. The NCCN Thyroid Carcinoma Clinical Practice Guidelines in Oncology (version 1.2021 – April 9, 2021). © 2021 National Comprehensive Cancer Network. Available at: http://www.nccn.org/. Accessed on July 16, 2021.
5. The NCCN Ovarian Cancer Clinical Practice Guidelines in Oncology (version 2.2022 – July 13, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org/. Accessed on July 25, 2022.
6. 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 July 22, 2022.
7. The NCCN Central Nervous System Cancers Clinical Practice Guidelines in Oncology (version 1.2022 – June 2, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org/. Accessed on July 11, 2022.
8. The NCCN Hepatobiliary Cancers Clinical Practice Guidelines in Oncology (version 2.2022 – July 15, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org/. Accessed on July 24, 2022.
9. The NCCN Ovarian Cancer, including Fallopian Tube Cancer and Primary Peritoneal Cancer Clinical Practice Guidelines in Oncology (version 2.2022 – July 13, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org/. Accessed on July 25, 2022.