PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Mekinist Prior Authorization Policy
- Mekinist® (trametinib tablets and oral solution – Novartis)

REVIEW DATE: 04/24/2024

INSTRUCTIONS FOR USE

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CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Mekinist, a kinase inhibitor, is indicated for the treatment of patients with the following conditions:[1]

- **Low-grade glioma,** in combination with Tafinlar® (dabrafenib capsules and tablets for oral suspension), for the treatment of pediatric patients ≥ 1 year of age with a *BRAF V600E* mutation who require systemic therapy.
- **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, 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.
- **Non-small cell lung cancer**, in combination with Tafinlar, for disease that has the *BRAF V600E* mutation as detected by an FDA-approved test.
- **Solid tumors – unresectable or metastatic**, in combination with Tafinlar, 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 Tafinlar, for locally advanced or metastatic anaplastic disease with *BRAF V600E* mutation and with no satisfactory locoregional treatment options.

Limitations of Use: Mekinist is not indicated for treatment of patients with colorectal cancer because of known intrinsic resistance to BRAF inhibition.

Dosing: For the tablet dosage form, Mekinist 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 of Mekinist 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, 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 1.2024 – February 26, 2024) 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 1.2024 – March 15, 2024) recommend Cotellic as "preferred" or Mekinist as "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 histiocytosis (including multisystem, pulmonary or central nervous system lesions), Erdheim-Chester disease, and Rosai-Dorfman disease.[6]
- **Melanoma, Cutaneous:** Guidelines (version 2.2024 – April 3, 2024) 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 5.2024 – April 23, 2024) 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[8] recommends use of Mekinist, in combination with Tafinlar, for the following *BRAF V600* positive tumors (all category 2A): High-grade gliomas, ampullary adenocarcinoma, neuroendocrine tumors, occult primary, pancreatic adenocarcinoma, salivary gland tumors, esophageal and esophagogastric junction cancers, gastric cancer, hairy cell leukemia, biliary tract cancers, gastrointestinal stromal tumors, brain metastases due to melanoma, ovarian cancer, small bowel adenocarcinoma, and differentiated thyroid carcinoma. NCCN Compendium also recommends use of Tafinlar as monotherapy for low-grade serous ovarian cancer.

POLICY STATEMENT

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

- **Mekinist® (trametinib tablets and oral solution – 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 ALL of 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 Tafinlar (dabrafenib capsules or tablets for oral suspension); AND
   D) Patient requires systemic therapy.

2. **Melanoma.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) 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.
   B) Patient has *BRAF V600* mutation-positive disease.

3. **Non-Small Cell Lung Cancer.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Patient has *BRAF V600* mutation-positive disease; AND
   B) The medication is prescribed in combination with Tafinlar (dabrafenib capsules or tablets for oral suspension).

4. **Solid Tumors – Unresectable or Metastatic.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
   Note: Examples of solid tumors are: biliary tract cancer, brain metastases due to melanoma, high-grade gliomas, differentiated thyroid carcinoma, gastrointestinal stromal tumors, gastric cancer, esophageal and esophagogastric junction cancers, salivary gland tumors, pancreatic adenocarcinoma, neuroendocrine tumors, occult primary, 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 Tafinlar (dabrafenib capsules or tablets for oral suspension); 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 ALL of the following (A, B, and C):
   A) Patient has locally advanced or metastatic anaplastic disease; AND
   B) Patient has *BRAF V600* mutation-positive disease; AND
   C) The medication is prescribed in combination with Tafinlar (dabrafenib capsules or tablets for oral suspension), unless intolerant.

Other Uses with Supportive Evidence

6. Hairy Cell Leukemia. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
- **A)** Patient has not been previously treated with a BRAF inhibitor therapy; AND
- **B)** The medication will be used for relapsed/refractory disease; AND
- **C)** The medication will be taken in combination with Tafinlar (dabrafenib capsules or tablets for oral suspension).

7. Histiocytic Neoplasm. Approve for 1 year if the patient meets ONE of the following (A, B, or C):
- **A)** Patient has Langerhans cell histiocytosis and one of the following (i, ii, or iii):
  - **i.** Multisystem disease; OR
  - **ii.** Pulmonary disease; OR
  - **iii.** Central nervous system lesions; OR
- **B)** Patient has Erdheim-Chester disease; OR
- **C)** Patient has Rosai-Dorfman disease.

8. Ovarian, Fallopian Tube, or Primary Peritoneal Cancer. Approve for 1 year if the patient meets BOTH of the following (A and B):
- **A)** Patient has recurrent disease; AND
- **B)** Patient meets ONE of the following (i or ii):
  - **i.** The medication is used for low-grade serous carcinoma; OR
  - **ii.** 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 or tablets for oral suspension).

9. Small Bowel Adenocarcinoma. Approve for 1 year if the patient meets BOTH of the following (A and B):
- **A)** Patient meets BOTH of the following (i and ii):
  - **i.** Patient has *BRAF V600E* mutation-positive advanced or metastatic disease; AND
  - **ii.** The medication will be taken in combination with Tafinlar (dabrafenib capsules or tablets for oral suspension); AND
- **B)** Patient meets ONE of the following (i or ii):
  - **i.** Patient meets BOTH of the following (a and b):
    - **a)** The medication will be used as initial therapy; AND
    - **b)** Patient has received previous FOLFOX/CAPEOX therapy in the adjuvant setting within the past 12 months or has a contraindication; OR
  - **ii.** The medication will be used as second-line and subsequent therapy.

CONDITIONS NOT COVERED

- **Mekinist® (trametinib tablets and oral solution – 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. Mekinist is not indicated for treatment of patients with colorectal cancer because of known intrinsic resistance to BRAF inhibition.[1]

REFERENCES

1. Mekinist® tablets and oral solution [prescribing information]. East Hanover, NJ: Novartis; August 2023.
2. The NCCN Melanoma: Cutaneous Clinical Practice Guidelines in Oncology (version 2.2024 – April 3, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org/. Accessed on April 22, 2024.
3. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (version 5.2024 – April 23, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org/. Accessed on April 23, 2024.
4. The NCCN Thyroid Carcinoma Clinical Practice Guidelines in Oncology (version 2.2024 – March 12, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org/. Accessed on April 22, 2024.
5. The NCCN Histiocytic Neoplasms Clinical Practice Guidelines in Oncology (version 1.2024 – March 15, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org/. Accessed on April 22, 2024.
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 22, 2024.
7. The NCCN Pediatric Central Nervous System Cancers Clinical Practice Guidelines in Oncology (version 1.2024 – February 26, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org/. Accessed on April 22, 2024.
8. The NCCN Drugs & Biologics Compendium. © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 7, 2024. Search term: trametinib.

HISTORY

Type of Revision	Summary of Changes	Review Date
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 solution 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 and Central Nervous System Cancer since they are now listed as examples under FDA-approved use "Solid Tumors – Unresectable or Metastatic" condition. Histiocytic Neoplasm and Ovarian Cancer (due to low-grade serous carcinoma) conditions were not deleted because Mekinist can be used as single agent in these settings (Solid Tumor indication requires use with Tafinlar).	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
Annual Revision	**Melanoma:** Deleted age criterion ≥ 6 years of age. **Non-Small Cell Lung Cancer:** Deleted age criterion ≥ 6 years of age. **Solid Tumors – Unresectable or Metastatic:** Added "occult primary" to the list of examples of solid tumors in the Note. **Thyroid Carcinoma, Anaplastic:** Deleted age criterion ≥ 6 years of age. **Histiocytic Neoplasm:** Deleted age criterion ≥ 6 years of age. **Ovarian, Fallopian Tube, or Primary Peritoneal Cancer:** Deleted age criterion ≥ 6 years of age. **Hairy Cell Leukemia:** Added new indication and criteria based on Compendium recommendations. **Small Bowel Adenocarcinoma:** Added new indication and criteria based on Compendium recommendations.	04/24/2024