Clinical Policy: Trametinib (Mekinist)

Reference Number: ERX.SPA.199
Effective Date: 01.11.17
Last Review Date: 05.22
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Trametinib (Mekinist®) is a kinase inhibitor.

FDA Approved Indication(s)
Mekinist is indicated:

- As a single agent for the treatment of BRAF-inhibitor treatment-naïve patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test
- In combination with dabrafenib (Tafinlar®):
  - For the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test
  - For the adjuvant treatment of patients with melanoma with BRAF V600E or V600K mutations, as detected by an FDA-approved test, and involvement of lymph node(s), following complete resection
  - For the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with BRAF V600E mutation as detected by an FDA-approved test
  - For the treatment of patients with locally advanced or metastatic anaplastic thyroid cancer (ATC) with BRAF V600E mutations and with no satisfactory locoregional treatment options
  - For the treatment of adult and pediatric patients 6 years of age and older with unresectable or metastatic solid tumors with BRAF V600E mutation who have progressed following prior treatment and have no satisfactory alternative treatment options.*

Limitation(s) of use: Mekinist is not indicated for treatment of patients with colorectal cancer because of known intrinsic resistance to BRAF inhibition.

** This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).*

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Mekinist is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Melanoma (must meet all)**:**

1. Diagnosis of melanoma with BRAF V600E or V600K mutation;
2. Disease meets one of the following (a or b):
   a. Unresectable, limited resectable, or metastatic;
   b. Presence of lymph node(s) involvement following complete resection;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. Request meets one of the following (a or b):*
   a. Dose does not exceed 2 mg (1 tablet) per day;

b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence)*.

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid – 6 months
Commercial – Length of Benefit

B. Non-Small Cell Lung Cancer (must meet all)**:**

1. Diagnosis of advanced, metastatic, or recurrent NSCLC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is positive for a BRAF V600E mutation;
5. Prescribed in combination with Tafinlar;
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 2 mg (1 tablet) per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence)*.

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid – 6 months
Commercial – Length of Benefit

C. Anaplastic Thyroid Cancer (must meet all)**:**

1. Diagnosis of advanced or metastatic ATC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is positive for a BRAF V600E mutation;
5. Prescribed in combination with Tafinlar;
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 2 mg (1 tablet) per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence)*.

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid – 6 months
Commercial – Length of Benefit

D. BRAF V600E Mutation-Positive Solid Tumor (must meet all):

1. Diagnosis of unresectable or metastatic solid tumor that is positive for a BRAF V600E mutation (*see Appendix D for examples*);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 6 years;
4. Disease has progressed on prior treatment, and no satisfactory alternative treatment options are available;
5. Prescribed in combination with Tafinlar;
6. Request meets one of the following (a or b):
   a. Dose does not exceed one of the following (i, ii, or iii):
      i. Adults or pediatric patients weighing ≥ 51 kg: 2 mg (1 tablet) per day;
      ii. Pediatric patients weighing 26-37 kg: 1 mg (2 tablets) per day;
      iii. Pediatric patients weighing 38-50 kg: 1.5 mg (3 tablets) per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid – 6 months
Commercial – Length of Benefit

E. Off-Label NCCN Compendium Recommended Indications (must meet all)**:**
1. Prescribed for one of the following (a-e):
   a. Metastatic uveal melanoma as a single agent;
   b. Epithelial ovarian cancer, fallopian tube cancer, or primary peritoneal cancer as a single agent;
   c. One of the following central nervous system cancers (i, ii, or iii):
      a. Adult low-grade (WHO Grade 1 or 2) glioma;
      b. Recurrent anaplastic glioma;
      c. Recurrent glioblastoma;
   d. One of the following hepatobiliary cancers, as subsequent treatment in unresectable or metastatic disease (i, ii, or iii):
      a. Extrahepatic cholangiocarcinoma;
      b. Gallbladder cancer;
      c. Intrahepatic cholangiocarcinoma;
   e. One of the following histiocytic neoplasms, prescribed as a single agent (i, ii, or iii):
      a. Erdheim-Chester disease;
      b. Langerhans cell histiocytosis;
      c. Rosai Dorfman disease;
2. Prescribed by or in consultation with one of the following (a or b):
   a. For histiocytic neoplasm: a hematologist or oncologist;
   b. For all other off-label cancers: an oncologist;
3. Age ≥ 18 years;
4. For epithelial ovarian cancer, fallopian tube cancer, or primary peritoneal cancer: Request is for recurrence therapy (e.g., previous treatment with a regimen containing carboplatin, cisplatin, or oxaliplatin) for low-grade serous carcinoma;
5. For central nervous system or hepatobiliary cancer: both of the following (a and b):
   a. Disease is positive for a BRAF V600E mutation;
   b. Prescribed in combination with Tafinlar;
6. For histiocytic neoplasms: Disease is positive for a MAP kinase pathway mutation, or no detectable mutation, or testing is not available;
7. Request meets one of the following (a or b):*
   a. Dose does not exceed 2 mg (1 tablet) per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence)*.

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid – 6 months
Commercial – Length of Benefit

F. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Mekinist for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed one of the following (i or ii);
      i. BRAF V600E mutation-positive solid tumor (1, 2, or 3):
         1) Adults or pediatric patients weighing ≥ 51 kg: 2 mg (1 tablet) per day;
         2) Pediatric patients weighing 26-37 kg: 1 mg (2 tablets) per day;
         3) Pediatric patients weighing 38-50 kg: 1.5 mg (3 tablets) per day;

ii. All other indications: 2 mg (1 tablet) per day;

b. New dose is supported by practice guideline or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid – 12 months
Commercial – Length of Benefit

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ATC: anaplastic thyroid cancer
BRAF: B-Raf proto-oncogene serine/threonine kinase
FDA: Food and Drug Administration
MAP: mitogen-activated protein
NSCLC: non-small cell lung cancer

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: General Information

- According to NCCN, Mekinist has category 2A recommendation for combination treatment with Tafinlar for brain metastases if active against primary tumor (melanoma) for recurrent disease.
- Examples of solid tumors that may be BRAF V600E mutation-positive include, but are not limited to, the following: biliary tract cancer, high grade glioma (glioblastoma, anaplastic pleomorphic xanthoastrocytoma, anaplastic astrocytoma, astroblastoma, anaplastic ganglioglioma, and anaplastic oligodendroglioma), low grade glioma (astrocytoma, ganglioglioma, pleomorphic xanthoastrocytoma, pilocytic astrocytoma, choroid plexus papilloma, gangliocytoma/ganglioglioma), adenocarcinoma of small intestine, pancreas, or anus, mixed ductal/adenoneuroendocrine carcinoma, neuroendocrine carcinoma of colon, ameloblastoma of mandible, combined small cell-squamous carcinoma of lung, mucinous-papillary serous adenocarcinoma of peritoneum, gastrointestinal stromal tumor.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Melanoma, NSCLC, ATC	2 mg (1 tablet) PO QD The recommended duration of treatment in the adjuvant melanoma setting is until disease recurrence or unacceptable toxicity for up to 1 year. The recommended duration of treatment for all other indications is until disease progression or unacceptable toxicity.	2 mg/day
BRAF V600E	Adults: 2 mg (1 tablet) PO QD	2 mg/day

Indication	Dosing Regimen	Maximum Dose
mutation-positive solid tumors	Pediatric patients: • 26-37 kg: 1 mg (two 0.5 mg tablets) PO QD • 38-50 kg: 1.5 mg (three 0.5 mg tablets) PO QD • ≥ 51 kg: 2 mg PO QD The recommended duration of treatment is until disease progression or unacceptable toxicity.	

VI. Product Availability

Tablets: 0.5 mg, 2 mg

VII. References

1. Mekinist Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; June 2022. Available at: www.pharma.us.novartis.com/product/pi/pdf/mekinist.pdf. Accessed July 11, 2022.
2. Trametinib. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at NCCN.org. Accessed February 18, 2022.
3. National Comprehensive Cancer Network. Cutaneous Melanoma Version 2.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cutaneous_melanoma.pdf. Accessed February 18, 2022.
4. National Comprehensive Cancer Network. Central Nervous System Cancers Version 2.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf. Accessed February 18, 2022.
5. National Comprehensive Cancer Network Guidelines. Non-Small Cell Lung Cancer Version 1.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed February 18, 2022.
6. National Comprehensive Cancer Network Guidelines. Thyroid Carcinoma Version 3.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf. Accessed February 18, 2022.
7. National Comprehensive Cancer Network. Uveal Melanoma Version 2.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/uveal.pdf. Accessed February 18, 2022.
8. National Comprehensive Cancer Network. Ovarian Cancer Version 1.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf. Accessed February 18, 2022.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2018 annual review: Added oncologist requirement; Removed NCCN recommendations, as FDA indication covers those recommendations; Added allowance for COC; Increased all approval durations to length of benefit; References reviewed and updated.	02.06.18	05.18
Criteria added for new FDA indications: anaplastic thyroid cancer and the adjuvant treatment of melanoma following complete lymph node(s) resection; added off-label use for uveal melanoma; references reviewed and updated.	05.29.18	08.18
2Q 2019 annual review: no significant changes; references reviewed and updated.	02.26.19	05.19
2Q 2020 annual review: added Medicaid line of business with 6/12 month initial/continued authorization duration; added NCCN supported off-label uses in ovarian, colon, and rectal cancers; added NCCN supported off-label dosing verbiage; for uveal melanoma removed unresectable disease to align with NCCN Compendium; for NSCLC added advanced disease; references reviewed and updated.	02.10.20	05.20
2Q 2021 annual review: removed colorectal cancer off-label use as it is no longer included in the NCCN Compendium; references reviewed and updated.	01.12.21	05.21
2Q 2022 annual review: added “limited resectable” melanoma classification per NCCN; clarified thyroid cancer should be advanced or metastatic per	02.21.22	05.22

Reviews, Revisions, and Approvals	Date	P&T Approval Date
NCCN; added indications of central nervous system cancers, hepatobiliary cancers, and histiocytic neoplasms per NCCN; references reviewed and updated.		
RT4: revised criteria to include new FDA-approved indication of BRAF V600E mutation-positive solid tumors.	07.11.22	

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.