Clinical Policy: Trametinib (Mekinist)

Reference Number: CP.PHAR.240
Effective Date: 07.01.16
Last Review Date: 05.22
Line of Business: Commercial, HIM, 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 mutation 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.

It is the policy of health plans affiliated with Centene Corporation® 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), disease is:
   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. For Mekinist requests, member must use generic trametinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
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/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

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. For Mekinist requests, medical justification supports inability to use generic trametinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
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/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

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. For Mekinist requests, member must use generic trametinib, if available, unless contraindicated or clinically significant adverse effects are experienced;

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/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

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. For Mekinist requests, member must use generic trametinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. 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/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

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):
      i. Adult low-grade (WHO Grade 1 or 2) glioma;
      ii. Recurrent anaplastic glioma;
      iii. Recurrent glioblastoma;
   d. One of the following hepatobiliary cancers, as subsequent treatment in unresectable or metastatic disease (i, ii, or iii):
      i. Extrahepatic cholangiocarcinoma;
      ii. Gallbladder cancer;
      iii. Intrahepatic cholangiocarcinoma;
   e. One of the following histiocytic neoplasms, prescribed as a single agent (i, ii, or iii):

i. Erdheim-Chester Disease;
ii. Langerhans Cell Histiocytosis;
iii. 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. For Mekinist requests, member must use generic trametinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
8. 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/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit, 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. For Mekinist requests, member must use generic trametinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
4. 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 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/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid 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 mutation-positive solid tumors	Adults: 2 mg (1 tablet) PO QD 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.	2 mg/day

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: no significant changes; policies combined for Commercial and Medicaid; added age; summarized NCCN and FDA approved uses for improved clarity; added specialist involvement in care; added continuity of care statement and updated approval duration from 3/6 to 6/12 months for Medicaid; references reviewed and updated.	02.06.18	05.18
Updated criteria with new indications for anaplastic thyroid cancer and the adjuvant treatment of melanoma following complete lymph node(s) resection; added off-label use for uveal melanoma; added TBD-HIM line of business.	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 NCCN supported off-label uses in ovarian, colon, and rectal cancers; added NCCN supported off-label dosing verbiage; for uveal melanoma removed unresectable disease	02.10.20	05.20

Reviews, Revisions, and Approvals	Date	P&T Approval Date
to align with NCCN Compendium; for NSCLC added advanced disease; references reviewed and updated.		
2Q 2021 annual review: removed colorectal cancer off-label use as it is no longer included in the NCCN Compendium; oral oncology generic redirection language added; revised reference to HIM off-label use policy from HIM.PHAR.21 to HIM.PA.154; 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 NCCN; added indications of central nervous system cancers, hepatobiliary cancers, and histiocytic neoplasms per NCCN; Commercial approval duration revised from "Length of Benefit" to "12 months or duration of request, whichever is less"; references reviewed and updated.	02.21.22	05.22
RT4: revised criteria to include new FDA-approved indication of BRAF V600E mutation-positive solid tumors.	07.11.22	
Template changes applied to other diagnoses/indications and continued therapy section.	10.10.22	

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a

discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.