# Mekinist® (trametinib)
## (Oral)

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## I. Length of Authorization

Coverage is provided for six months and may be renewed.

## II. Dosing Limits

**A. Quantity Limit (max daily dose) [Pharmacy Benefit]:**

- Mekinist 0.5 mg tablet: 3 tablets per day
- Mekinist 2 mg tablet: 1 tablet per day

**B. Max Units (per dose and over time) [Medical Benefit]:**

- 2 mg daily

## III. Initial Approval Criteria

Coverage is provided in the following conditions:

- Baseline left ventricular ejection fraction (LVEF) within normal limits; **AND**
- Patient is at least 18 years or older; **AND**
- Patient has not received prior therapy with BRAF and/or MEK inhibitors (e.g., vemurafenib, encorafenib, cobimetinib, binimetinib, etc.) unless otherwise specified; **AND**

**Melanoma †**

- Patient has BRAF V600E or V600K mutation detected by FDA approved test*; **AND**
  - Used in combination with dabrafenib as adjuvant therapy for patients with lymph node involvement, following complete resection; **OR**
  - Used in combination with dabrafenib or as a single agent (if BRAF/MEK inhibitor combination therapy is contraindicated); **AND**
    - Patient's disease is unresectable OR metastatic; **AND**
    - Used as initial therapy or subsequent therapy; **OR**
    - Used as re-induction therapy for progression/relapse in patients who had disease control for >3 months after previous therapy with trametinib ‡; **OR**

- Used as single agent for the treatment of unresectable or metastatic Uveal Melanoma ‡

**Anaplastic Thyroid Cancer (ATC) †**

- Patient has BRAF V600E mutation detected by FDA approved test*; **AND**
- Used in combination with dabrafenib; **AND**
  - Used for locally advanced or metastatic disease with no satisfactory locoregional treatment options; **OR**
  - Used adjuvantly for locoregional disease following R0 or R1 resection

**Non-Small Cell Lung Cancer †**

- Patient has BRAF V600E mutation as detected by FDA approved test*; **AND**
- Patient has recurrent or metastatic disease; **AND**
- Used in combination with dabrafenib

**Central Nervous System Cancers – Brain Metastases ‡**

- Patient's primary cancer is BRAF V600E or V600K mutation positive melanoma; **AND**
- Used in combination with dabrafenib; **AND**
  - Patient has newly diagnosed or stable systemic disease or reasonable systemic treatment options; **OR**
  - Patient has recurrent brain metastases.

*http://www.fda.gov/CompanionDiagnostics

† FDA Approved Indication(s); ‡ Compendia Approved Indication(s)

## IV. Renewal Criteria

Coverage can be renewed based upon the following criteria:

- Patient continues to meet the criteria identified in Section III; **AND**
- Tumor response with stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: interstitial lung disease/pneumonitis; cardiomyopathy; cutaneous/non-cutaneous malignancies; severe hemorrhagic events; colitis/gastrointestinal perforation; venous thromboembolism; persistent retinal pigment epithelial detachment (RPED); retinal vein occlusion (RVO); skin toxicity; serious febrile reactions; hyperglycemia; etc. **AND**
- Left ventricular ejection fraction (LVEF) has not had an absolute decrease from baseline ≥ 10% and is not below the lower limit of normal (LLN)

**Adjuvant treatment of Melanoma**

- Treatment has not exceeded 1 year of therapy

**Melanoma (metastatic or unresectable disease)**

- Patient has completed initial induction; **AND**
- Used as re-induction therapy in patients who experienced disease control, but subsequently disease progression/relapse > 3 months after treatment discontinuation

## V. Dosage/Administration

| Indication | Dose |
|---|---|
| All indications | 2 mg orally once daily |

## VI. Billing Code/Availability Information

Jcode:

- J8999 – Prescription drug oral, chemotherapeutic, Not Otherwise Specified
- C9399 – Unclassified drug or biological (Hospital Outpatient Use Only)

NDC:

- Mekinist 0.5 mg tablet: 00078-0666-xx
- Mekinist 2 mg tablet: 00078-0668-xx

## VII. References


1. Mekinist [package insert]. East Hanover, NJ; Novartis Pharmaceuticals Corporation; May 2018. Accessed October 2018.
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3. Flaherty KT, Infante JR, Daud A, at al. Combined BRAF and MEK inhibition in melanoma with BRAF V600 mutations. N Engl J Med. 2012 Nov; 367(18):1694-703. doi: 10.1056/NEJMoa1210093. Epub 2012 Sep 29.
4. Kim KB, Kefford R, Pavlick AC, et al. Phase II study of the MEK1/MEK2 inhibitor Trametinib in patients with metastatic BRAF-mutant cutaneous melanoma previously treated with or without a BRAF inhibitor. J Clin Oncol. 2013 Feb 1; 31(4):482-9.
5. Long GV, Stroyakovksy D, Gogas H, et al. Combined BRAF and MEK inhibition versus BRAF inhibition alone in melanoma. N Eng J Med 2014 Sep 29, {Epub ahead of print]
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7. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) trametinib. National Comprehensive Cancer Network, 2018. The NCCN

Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed October 2018.

8. Planchard D, Groen HJM, Min Kim T., et al. Interim results of a phase II study of the BRAF inhibitor dabrafenib in combination with the MEK inhibitor trametinib in patients with BRAF V600E mutated metastatic non-small cell lung cancer. Journal of Clinical Oncology, 2015; 33 Abstract 8006.
9. Davies, MA, Salag P, Robert C, et al. Dabrafenib plus trametinib in patients with BRAFV600-mutant melanoma brain metastases (COMBI-MB): a multicentre, multicohort, open-label, phase 2 trial The Lancet Oncology. 2017:18 (7):863-873.
10. Falchook GS, Lewis KD, Infante JR, et al. Activity of the MEK Inhibitor Trametinib (GSK1120212) in Advanced Melanoma in a Phase I, Dose-escalation Trial. The lancet oncology. 2012;13(8):782-789. doi:10.1016/S1470-2045(12)70269-3.
11. Shoushtari N, Kudchadkar RR, Panageas K, et al. A randomized phase 2 study of trametinib with or without GSK2141795 in patients with advanced uveal melanoma. Journal of Clinical Oncology 2016 34:15_suppl, 9511-9511.

## Appendix 1 – Covered Diagnosis Codes

| ICD-10 | ICD-10 Description |
|---|---|
| C33 | Malignant neoplasm of trachea |
| C34.00 | Malignant neoplasm of unspecified main bronchus |
| C34.01 | Malignant neoplasm of right main bronchus |
| C34.02 | Malignant neoplasm of left main bronchus |
| C34.10 | Malignant neoplasm of upper lobe, unspecified bronchus or lung |
| C34.11 | Malignant neoplasm of upper lobe, right bronchus or lung |
| C34.12 | Malignant neoplasm of upper lobe, left bronchus or lung |
| C34.2 | Malignant neoplasm of middle lobe, bronchus or lung |
| C34.30 | Malignant neoplasm of lower lobe, unspecified bronchus or lung |
| C34.31 | Malignant neoplasm of lower lobe, right bronchus or lung |
| C34.32 | Malignant neoplasm of lower lobe, left bronchus or lung |
| C34.80 | Malignant neoplasm of overlapping sites of unspecified bronchus or lung |
| C34.81 | Malignant neoplasm of overlapping sites of right bronchus and lung |
| C34.82 | Malignant neoplasm of overlapping sites of left bronchus and lung |
| C34.90 | Malignant neoplasm of unspecified part of unspecified bronchus or lung |
| C34.91 | Malignant neoplasm of unspecified part of right bronchus or lung |
| C34.92 | Malignant neoplasm of unspecified part of left bronchus or lung |

| ICD-10 | ICD-10 Description |
|---|---|
| C43.0 | Malignant melanoma of lip |
| C43.10 | Malignant melanoma of unspecified eyelid, including canthus |
| C43.11 | Malignant melanoma of right eyelid, including canthus |
| C43.12 | Malignant melanoma of left eyelid, including canthus |
| C43.20 | Malignant melanoma of unspecified ear and external auricular canal |
| C43.21 | Malignant melanoma of right ear and external auricular canal |
| C43.22 | Malignant melanoma of left ear and external auricular canal |
| C43.30 | Malignant melanoma of unspecified part of face |
| C43.31 | Malignant melanoma of nose |
| C43.39 | Malignant melanoma of other parts of face |
| C43.4 | Malignant melanoma of scalp and neck |
| C43.51 | Malignant melanoma of anal skin |
| C43.52 | Malignant melanoma of skin of breast |
| C43.59 | Malignant melanoma of other part of trunk |
| C43.60 | Malignant melanoma of unspecified upper limb, including shoulder |
| C43.61 | Malignant melanoma of right upper limb, including shoulder |
| C43.62 | Malignant melanoma of left upper limb, including shoulder |
| C43.70 | Malignant melanoma of unspecified lower limb, including hip |
| C43.71 | Malignant melanoma of right lower limb, including hip |
| C43.72 | Malignant melanoma of left lower limb, including hip |
| C43.8 | Malignant melanoma of overlapping sites of skin |
| C43.9 | Malignant melanoma of skin, unspecified |
| C69.30 | Malignant neoplasm of unspecified choroid |
| C69.31 | Malignant neoplasm of right choroid |
| C69.32 | Malignant neoplasm of left choroid |
| C69.40 | Malignant neoplasm of unspecified ciliary body |
| C69.41 | Malignant neoplasm of right ciliary body |
| C69.42 | Malignant neoplasm of left ciliary body |
| C69.60 | Malignant neoplasm of unspecified orbit |
| C69.61 | Malignant neoplasm of right orbit |
| C69.62 | Malignant neoplasm of left orbit |
| C73 | Malignant neoplasm of thyroid gland |
| C79.31 | Secondary malignant neoplasm of brain |
| C80.0 | Disseminated malignant neoplasm, unspecified |

| ICD-10 | ICD-10 Description |
|---|---|
| C80.1 | Malignant (primary) neoplasm, unspecified |
| Z85.118 | Personal history of other malignant neoplasm of bronchus and lung |
| Z85.820 | Personal history of malignant melanoma of skin |

## Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD):

N/A

| Medicare Part B Administrative Contractor (MAC) Jurisdictions | | |
|---|---|---|
| **Jurisdiction** | **Applicable State/US Territory** | **Contractor** |
| E (1) | CA,HI, NV, AS, GU, CNMI | Noridian Healthcare Solutions, LLC |
| F (2 & 3) | AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ | Noridian Healthcare Solutions, LLC |
| 5 | KS, NE, IA, MO | Wisconsin Physicians Service Insurance Corp (WPS) |
| 6 | MN, WI, IL | National Government Services, Inc. (NGS) |
| H (4 & 7) | LA, AR, MS, TX, OK, CO, NM | Novitas Solutions, Inc. |
| 8 | MI, IN | Wisconsin Physicians Service Insurance Corp (WPS) |
| N (9) | FL, PR, VI | First Coast Service Options, Inc. |
| J (10) | TN, GA, AL | Palmetto GBA, LLC |
| M (11) | NC, SC, WV, VA (excluding below) | Palmetto GBA, LLC |
| L (12) | DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA) | Novitas Solutions, Inc. |
| K (13 & 14) | NY, CT, MA, RI, VT, ME, NH | National Government Services, Inc. (NGS) |
| 15 | KY, OH | CGS Administrators, LLC |