Reference number(s)
1681-A

Specialty Guideline Management
Mekinist

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Mekinist	trametinib

Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met, and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications[1]

- Mekinist is indicated, as a single agent in BRAF-inhibitor treatment-naïve patients or in combination with dabrafenib, for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test.
- Mekinist is indicated, in combination with dabrafenib, 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.
- Mekinist is indicated, in combination with dabrafenib, for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with BRAF V600E mutation as detected by an FDA-approved test.
- Mekinist is indicated, in combination with dabrafenib, for the treatment of patients with locally advanced or metastatic anaplastic thyroid cancer (ATC) with BRAF V600E mutation and no satisfactory locoregional treatment options.

- Mekinist is indicated, in combination with dabrafenib, for the treatment of adult and pediatric patients 1 year 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.
- Mekinist is indicated, in combination with dabrafenib, for the treatment of pediatric patients 1 year of age and older with low-grade glioma (LGG) with a BRAF V600E mutation who require systemic therapy.

Limitations of Use

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

Compendial Uses[2-9]

- Melanoma
  - Cutaneous Melanoma
  - Uveal Melanoma
- Non-Small Cell Lung Cancer (NSCLC)
- Thyroid Cancer
  - Follicular Thyroid Carcinoma
  - Oncocytic Thyroid Carcinoma
  - Papillary Thyroid Carcinoma
  - Anaplastic Thyroid Carcinoma
- Central Nervous System Cancer
  - Glioma, BRAF V600 activating mutation-positive
  - Meningioma, BRAF V600 activating mutation-positive
  - Astrocytoma, BRAF V600 activating mutation-positive
  - Brain Cancer and Neurofibromatosis Type 1
- Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer
- Biliary Tract Cancers
  - Gallbladder Cancer
  - Extrahepatic Cholangiocarcinoma
  - Intrahepatic Cholangiocarcinoma
- Ampullary Adenocarcinoma
- Histiocytic Neoplasms
  - Erdheim-Chester Disease
  - Langerhans Cell Histiocytosis
  - Rosai-Dorfman Disease
- Solid Tumors
- Gastrointestinal Stromal Tumor (GIST)
- Pancreatic Adenocarcinoma
- Salivary Gland Tumor
- Gastric Adenocarcinoma
- Esophageal and Esophagogastric Junction Cancer

- Hairy Cell Leukemia
- Small Bowel Adenocarcinoma
- Epithelioid Hemangioendothelioma

All other indications are considered experimental/investigational and not medically necessary.

Documentation

Submission of BRAF mutation documentation is necessary to initiate the prior authorization review for applicable indications as outlined in the coverage criteria section.

Coverage Criteria

Melanoma[1,2]

Authorization of 12 months may be granted for treatment of melanoma in any of the following settings:

- Unresectable or metastatic cutaneous melanoma when used either:
  - As single agent for subsequent therapy of disease that is BRAF gene fusion- and non-V600 mutation-positive, or
  - In combination with dabrafenib (Tafinlar) for BRAF V600 mutation positive disease, or
  - In combination with dabrafenib (Tafinlar) and pembrolizumab (Keytruda) as subsequent therapy for BRAF V600 positive disease
- Neoadjuvant treatment of stage III cutaneous melanoma with a BRAF V600 mutation in combination with dabrafenib (Tafinlar) if immunotherapy is contraindicated.
- Adjuvant treatment of resected stage III cutaneous melanoma with a BRAF V600 activating mutation in combination with dabrafenib (Tafinlar).
- Limited resectable local satellite/in-transit recurrent disease in combination with dabrafenib (Tafinlar).
- Uveal melanoma as a single agent for metastatic or unresectable disease.

Non-Small Cell Lung Cancer (NSCLC)[1,2]

Authorization of 12 months may be granted for treatment of BRAF V600E mutation-positive recurrent, advanced, or metastatic NSCLC in combination with dabrafenib (Tafinlar) when the member has not experienced disease progression on BRAF-targeted therapy.

Thyroid Cancer[1,2]

Authorization of 12 months may be granted for treatment of BRAF V600E mutation-positive follicular or papillary thyroid carcinoma in combination with dabrafenib (Tafinlar) if either of the following criteria is met:

- The requested medication will be used as subsequent therapy for unresectable or metastatic disease not amenable to radioactive iodine (RAI) therapy.
- The requested medication will be used as first-line systemic therapy for members with high-risk disease who are not appropriate for vascular endothelial growth factor (VEGF) inhibitors and not amenable to RAI therapy.

Authorization of 12 months may be granted for treatment of BRAF V600E mutation-positive oncocytic thyroid carcinoma in combination with Tafinlar (dabrafenib) if either of the following criteria is met:

- The requested medication will be used as subsequent therapy for unresectable or metastatic disease.
- The requested medication will be used as first-line therapy for members with high-risk disease who are not appropriate for vascular endothelial growth factor (VEGF) inhibitors.

Authorization of 12 months may be granted for treatment of BRAF V600E mutation-positive anaplastic thyroid carcinoma in combination with dabrafenib (Tafinlar) if either of the following criteria are met:

- The requested medication will be used as neoadjuvant therapy for borderline resectable stage IVa or IVb disease.
- The requested medication will be used for treatment of stage IVc disease.

Central Nervous System Cancer[2-8]

Authorization of 12 months may be granted for treatment of central nervous system cancer in a member with either of the following:

- BRAF V600 mutation-positive gliomas, meningiomas, or astrocytomas
- Brain cancer and neurofibromatosis type 1
- Brain metastases in BRAF V600E positive melanoma in combination with dabrafenib (Tafinlar)

Ovarian Cancer, Fallopian Tube Cancer, and Primary Peritoneal Cancer[2,10]

Authorization of 12 months may be granted for treatment of persistent or recurrent BRAF-V600E mutation positive epithelial ovarian cancer, fallopian tube cancer, primary peritoneal cancer, carcinosarcoma (malignant mixed Mullerian tumors), clear cell carcinoma of the ovary, or grade 1 endometrioid carcinoma, or mucinous carcinoma of the ovary in combination with dabrafenib (Tafinlar).

Authorization of 12 months may be granted for treatment of recurrent BRAF-V600E mutation-positive low-grade serous carcinoma/ovarian borderline epithelial tumors (low malignant potential) as a single agent or in combination with dabrafenib (Tafinlar).

Biliary Tract Cancers[2]

Authorization of 12 months may be granted for subsequent treatment of progressive BRAF-V600E mutation-positive unresectable, resected gross residual (R2), or metastatic gallbladder cancer,

extrahepatic cholangiocarcinoma, or intrahepatic cholangiocarcinoma in combination with dabrafenib (Tafinlar).

Ampullary Adenocarcinoma[2]

Authorization of 12 months may be granted for subsequent treatment of BRAF-V600E mutation-positive ampullary adenocarcinoma in combination with dabrafenib (Tafinlar).

Histiocytic Neoplasms[2]

Authorization of 12 months may be granted for treatment of Erdheim-Chester Disease, Langerhans Cell Histiocytosis, or Rosai-Dorfman Disease as a single agent.

Solid Tumors[1]

Authorization of 12 months may be granted for treatment of unresectable or metastatic solid tumors when all of the following criteria are met:

- The tumors are BRAF V600E mutation positive.
- The disease has progressed following prior treatment and there are no satisfactory alternative treatment options.
- The member is 1 year of age or older.
- The requested medication will not be used for the treatment of colorectal cancer.
- The requested medication will be used in combination with dabrafenib (Tafinlar).

Gastrointestinal Stromal Tumor (GIST)[2]

Authorization of 12 months may be granted for treatment of BRAF V600E mutation-positive GIST in combination with dabrafenib (Tafinlar) when used as either of the following:

- Neoadjuvant therapy
- First-line therapy for gross residual disease (R2 resection), unresectable primary disease, tumor rupture or recurrent/metastatic disease

Pancreatic Adenocarcinoma[2]

Authorization of 12 months may be granted for treatment of BRAF V600E mutation-positive pancreatic adenocarcinoma in combination with dabrafenib (Tafinlar) in the following settings:

- Treatment of locally advanced disease
- Subsequent treatment of recurrent or metastatic disease

Salivary Gland Tumors[2,9]

Authorization of 12 months may be granted for treatment of BRAF V600E mutation-positive recurrent, unresectable, or metastatic salivary gland tumors in combination with dabrafenib (Tafinlar).

Gastric, Esophageal and Esophagogastric Junction Cancer[2]

Authorization of 12 months may be granted for palliative treatment of BRAF V600E mutation-positive unresectable locally advanced, recurrent, or metastatic gastric, esophageal, and esophagogastric junction cancer or for members who are not surgical candidates, in combination with dabrafenib (Tafinlar).

Hairy Cell Leukemia[2]

Authorization of 12 months may be granted for treatment of relapsed/refractory hairy cell leukemia or previously treated hairy cell leukemia with incomplete hematologic recovery in combination with dabrafenib (Tafinlar), when the disease is BRAF V600E-mutation positive and the member has not previously been treated with BRAF inhibitor therapy.

Small Bowel Adenocarcinoma[2]

Authorization of 12 months may be granted for treatment of BRAF V600E mutation-positive advanced or metastatic small bowel adenocarcinoma in combination with dabrafenib (Tafinlar).

Epithelioid Hemangioendothelioma[2]

Authorization of 12 months may be granted as a single agent for treatment of epithelioid hemangioendothelioma.

Continuation of Therapy

Gastrointestinal Stromal Tumor (GIST)

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for treatment of GIST when there is no evidence of unacceptable toxicity while on the current regimen.

All Other Indications

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in the coverage criteria section when there is no evidence of unacceptable toxicity or disease progression or recurrence while on the current regimen. For patients using Mekinist for adjuvant treatment of cutaneous melanoma, only 12 months of therapy total will be approved.

References

1. Mekinist [package insert]. East Hanover, NJ: Novartis Pharmaceutical Corporation; April 2025.
2. The NCCN Drugs & Biologics Compendium® © 2025 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed November 18, 2025.
3. Usubalieva A, Pierson CR, Kavran CA, et al. Primary Meningeal Pleomorphic Xanthoastrocytoma With Anaplastic Features: A Report of 2 Cases, One With BRAFV600E Mutation and Clinical Response to the BRAF Inhibitor Dabrafenib. J Neuropathol Exp Neurol. 2015;74(10):960-969. doi:10.1097/NEN.0000000000000240.
4. Mordechai O, Postovsky S, Vlodavsky E, et al. Metastatic Rhabdoid Meningioma with BRAF V600E Mutation and Good Response to Personalized Therapy: Case Report and Review of the Literature. Pediatr Hematol Oncol. 2015; 32:3, 207-211, DOI: 10.3109/08880018.2014.936058
5. Lassaletta, A, Guerreiro Stucklin, A, Ramaswamy, V, et al. Profound clinical and radiological response to BRAF inhibition in a 2-month-old diencephalic child with hypothalamic/chiasmatic glioma. Pediatric Blood and Cancer. 2016; 63: 2038-2041. doi:10.1002/pbc.26086.
6. Meletath SK, Pavlick D, Brennan T, et al. Personalized Treatment for a Patient with a BRAF V600E Mutation using Dabrafenib and a Tumor Treatment Fields Device in a High-Grade Glioma Arising from Ganglioglioma. J Natl Compr Canc Netw. 2016;14(11):1345-1350.
7. Knight T, Shatara M, Carvalho L, et al. Dramatic response to trametinib in a male child with neurofibromatosis type 1 and refractory astrocytoma. Pediatr Blood Cancer. 2019; 66(1):e27474.
8. See WL, Tan IL, Mukherjee J, et al. Sensitivity of Glioblastomas to Clinically Available MEK Inhibitors Is Defined by Neurofibromin 1 Deficiency. Cancer Res. 2012;72(13):3350.
9. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Head and Neck Cancers. Version 5.2025. Accessed November 10, 2025. https://www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf
10. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer. Version 3.2025. Accessed November 18, 2025. https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf