

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 Indications¹

- 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.

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- 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 Uses²⁻⁹

- Melanoma (including brain metastases), BRAF V600 activating mutation-positive
- Glioma, BRAF V600 activating mutation-positive
- Meningioma, BRAF V600 activating mutation-positive
- Astrocytoma, BRAF V600 activating mutation-positive
- Uveal melanoma as a single agent
- Brain cancer and neurofibromatosis type 1
- Non-small cell lung cancer (NSCLC)
- Ovarian cancer/fallopian tube cancer/primary peritoneal cancer
- Biliary tract cancers
 - Gallbladder cancer
 - Extrahepatic cholangiocarcinoma
 - Intrahepatic cholangiocarcinoma
- Histiocytic neoplasms
 - Erdheim-Chester disease
 - Langerhans cell histiocytosis
 - Rosai-Dorfman disease
- Anaplastic thyroid carcinoma
- Follicular, oncocytic, papillary carcinoma
- Gastrointestinal stromal tumor
- Pancreatic adenocarcinoma
- Salivary gland tumor
- Gastric adenocarcinoma
- Esophageal and esophageal junction cancer
- Hairy cell leukemia
- Small bowel adenocarcinoma

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 subsequent therapy for disease that is BRAF gene fusion- and non-V600 mutation-positive, or
 - in combination with dabrafenib (Tafinlar) with or without pembrolizumab (Keytruda) for disease with a BRAF V600 activating mutation (e.g., V600E or V600K)
- Neoadjuvant treatment of BRAF V600 mutation-positive cutaneous melanoma 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.

Anaplastic Thyroid Cancer^{1,2}

Authorization of 12 months may be granted for treatment of BRAF V600E mutation-positive locally advanced or stage IV anaplastic thyroid carcinoma in combination with dabrafenib (Tafinlar).

Follicular, Oncocytic, and Papillary Thyroid Cancer²

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

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- The member has unresectable or metastatic disease not amenable to radioactive iodine (RAI) therapy.
- 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.

Central Nervous System Cancer²⁻⁸

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

Ovarian Cancer, Fallopian Tube Cancer, and Primary Peritoneal Cancer²

Authorization of 12 months may be granted for treatment of persistent or recurrent epithelial ovarian cancer, fallopian tube cancer, primary peritoneal cancer, carcinosarcoma (malignant mixed Mullerian tumors), clear cell carcinoma of the ovary, grade 1 endometrioid carcinoma, low-grade serous ovarian carcinoma/ ovarian borderline epithelial tumors (low malignant potential) or mucinous carcinoma of the ovary.

Biliary Tract Cancers²

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).

Histiocytic Neoplasms²

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 Tumors¹

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.

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- 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 Adenocarcinoma²

Authorization of 12 months may be granted for treatment of BRAF V600E mutation-positive recurrent, locally advanced, or metastatic disease in combination with dabrafenib (Tafinlar).

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 tumor in combination with dabrafenib (Tafinlar).

Gastric, Esophageal and Esophagogastric Junction Cancer²

Authorization of 12 months may be granted for subsequent treatment of BRAF V600E mutation-positive unresectable locally advanced, recurrent, or metastatic disease or for members who are not surgical candidates, in combination with dabrafenib (Tafinlar).

Hairy Cell Leukemia²

Authorization of 12 months may be granted for treatment of relapsed/refractory hairy cell leukemia in combination with dabrafenib (Tafinlar) if not previously treated with BRAF inhibitor therapy.

Small Bowel Adenocarcinoma

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).

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; October 2024.
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3. Usabalieva 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, Vlodaysky 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 5.2024. Accessed November 15, 2024. https://www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf