

# Specialty Guideline Management

## Tafinlar

### 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
Tafinlar	dabrafenib

### 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<sup>1</sup>

- Tafinlar is indicated as a single agent for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation as detected by an FDA-approved test.
- Tafinlar is indicated, in combination with trametinib, for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test.
- Tafinlar is indicated, in combination with trametinib, 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.
- Tafinlar is indicated, in combination with trametinib, for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with BRAF V600E mutation as detected by an FDA-approved test.

- Tafinlar is indicated, in combination with trametinib, for the treatment of patients with locally advanced or metastatic anaplastic thyroid cancer (ATC) with BRAF V600E mutation and no satisfactory locoregional treatment options.
- Tafinlar is indicated, in combination with trametinib, 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.
- Tafinlar is indicated, in combination with trametinib, 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

Tafinlar is not indicated for treatment of patients with colorectal cancer because of known intrinsic resistance to BRAF inhibition. Tafinlar is not indicated for treatment of patients with wild-type BRAF solid tumors.

## Compendial Uses<sup>2-8</sup>

- Melanoma, BRAF V600 activating mutation-positive
- NSCLC, BRAF V600E
- Glioma, BRAF V600 activating mutation-positive
- Meningioma, BRAF V600 activating mutation-positive
- Astrocytoma, BRAF V600 activating mutation-positive
- Anaplastic thyroid carcinoma
- Follicular, oncocytic, papillary carcinoma
- Biliary tract cancers
  - Gallbladder cancer
  - Extrahepatic cholangiocarcinoma
  - Intrahepatic cholangiocarcinoma
- Histiocytic neoplasms
  - Erdheim-Chester disease
  - Langerhans cell histiocytosis
- Ovarian cancer/fallopian tube cancer/primary peritoneal cancer
- 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 prior authorization review.

## Coverage Criteria

### Cutaneous Melanoma<sup>1,2</sup>

Authorization of 12 months may be granted for treatment of BRAF V600 mutation-positive (e.g., BRAF V600E or V600K mutations) melanoma in any of the following settings:

- Unresectable or metastatic disease when used either:
  - as a single agent if BRAF/MEK inhibitor combination therapy is contraindicated, or
  - in combination with trametinib (Mekinist) with or without pembrolizumab (Keytruda)
- Neoadjuvant therapy in combination with trametinib (Mekinist) if immunotherapy is contraindicated.
- Adjuvant treatment of resected stage III cutaneous melanoma in combination with trametinib (Mekinist).
- Limited resectable local satellite/in-transit recurrent disease in combination with trametinib (Mekinist).

### Non-Small Cell Lung Cancer (NSCLC)<sup>1-3</sup>

Authorization of 12 months may be granted for treatment of BRAF V600E mutation-positive recurrent, advanced, or metastatic NSCLC when the member has not experienced disease progression on BRAF-targeted therapy and the requested drug will be used either:

- as a single agent, if the combination of dabrafenib plus trametinib is not tolerated, or
- in combination with trametinib (Mekinist)

### Central Nervous System Cancer<sup>1,2,4-7</sup>

Authorization of 12 months may be granted for treatment of BRAF V600 mutation-positive gliomas, meningiomas, or astrocytomas.

### Anaplastic Thyroid Cancer<sup>1-2</sup>

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 trametinib (Mekinist).

## Follicular, Oncocytic, and Papillary Thyroid Cancer<sup>2</sup>

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

- 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.

## Biliary Tract Cancers<sup>2</sup>

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 trametinib (Mekinist).

## Histiocytic Neoplasms<sup>2</sup>

Authorization of 12 months may be granted for treatment of BRAF V600E mutation-positive Erdheim-Chester disease or Langerhans cell histiocytosis as a single agent.

## Solid Tumors<sup>1</sup>

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 trametinib (Mekinist).

## Ovarian Cancer, Fallopian Tube Cancer, and Primary Peritoneal Cancer<sup>2</sup>

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, grade 1 endometrioid carcinoma, low-grade serious carcinoma/ovarian borderline epithelial tumor (low malignant potential), or mucinous carcinoma of the ovary, in combination with trametinib (Mekinist).

## Gastrointestinal Stromal Tumor (GIST)<sup>2</sup>

Authorization of 12 months may be granted for treatment of BRAF V600E mutation-positive GIST in combination with trametinib (Mekinist) 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<sup>2</sup>

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

## Salivary Gland Tumors<sup>2,8</sup>

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

## Gastric, Esophageal and Esophagogastric Junction Cancer<sup>2</sup>

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 trametinib (Mekinist).

## Hairy Cell Leukemia<sup>2</sup>

Authorization of 12 months may be granted for treatment of relapsed/refractory hairy cell leukemia in combination with trametinib (Mekinist) 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 trametinib (Mekinist).

# 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 continued treatment in members requesting reauthorization for an indication listed 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 Tafenlar for adjuvant treatment of cutaneous melanoma, only 12 months of therapy total will be approved.

## References

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4. 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. *Journal of neuropathology and experimental neurology*. 2015;74(10):960-969. doi:10.1097/NEN.0000000000000240.
5. 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. *Pediatric Hematology and Oncology*. 2015; 32:3, 207-211, DOI: 10.3109/08880018.2014.936058
6. 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.
7. 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. *Journal of the National Comprehensive Cancer Network*. 2016; 14(11): 1345-1350.
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