Reference number(s)
1683-A

SPECIALTY GUIDELINE MANAGEMENT

TAFINLAR (dabrafenib)

POLICY

I. 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.

A. FDA-Approved Indications
1. 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.
2. 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.
3. 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.
4. 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.
5. 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.
6. 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.
7. 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.

B. Compendial Uses
1. Melanoma, BRAF V600 activating mutation-positive
2. Brain metastases from melanoma
3. NSCLC, BRAF V600E
4. Glioma, BRAF V600 activating mutation-positive
5. Meningioma, BRAF V600 activating mutation-positive
6. Astrocytoma, BRAF V600 activating mutation-positive
7. Anaplastic thyroid carcinoma
8. Biliary tract cancers
   a. Gallbladder cancer
   b. Extrahepatic cholangiocarcinoma
   c. Intrahepatic cholangiocarcinoma
9. Histiocytic neoplasms
   a. Erdheim-Chester disease

   b. Langerhans cell histiocytosis
10. Ovarian cancer/fallopian tube cancer/primary peritoneal cancer
11. Gastrointestinal stromal tumor
12. Pancreatic adenocarcinoma
13. Salivary gland tumor
14. Gastric adenocarcinoma
15. Esophageal and esophageal junction cancer
16. Hairy cell leukemia
17. Small bowel adenocarcinoma

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

II. DOCUMENTATION

Submission of BRAF mutation documentation is necessary to initiate prior authorization review.

III. CRITERIA FOR INITIAL APPROVAL

A. Cutaneous Melanoma

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:

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

B. Non-Small Cell Lung Cancer (NSCLC)

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:

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

C. Central Nervous System Cancer

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

D. Anaplastic Thyroid Cancer

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).

E. Biliary Tract Cancers

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).

F. Histiocytic Neoplasms
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.

G. Solid Tumors
Authorization of 12 months may be granted for treatment of unresectable or metastatic solid tumors when all of the following criteria are met:
1. The tumors are BRAF V600E mutation positive.
2. The disease has progressed following prior treatment and there are no satisfactory alternative treatment options.
3. The member is 1 year of age or older.
4. The requested medication will not be used for the treatment of colorectal cancer.
5. The requested medication will be used in combination with trametinib (Mekinist).

H. Ovarian Cancer, Fallopian Tube Cancer, and Primary Peritoneal Cancer
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).

I. Gastrointestinal Stromal Tumor (GIST)
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:
1. Neoadjuvant therapy
2. First-line therapy for gross residual disease (R2 resection), unresectable primary disease, tumor rupture or recurrent/metastatic disease

J. Pancreatic Adenocarcinoma
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).

K. Salivary Gland Tumors
Authorization of 12 months may be granted for treatment of BRAF V600E mutation-positive recurrent salivary gland tumor in combination with trametinib (Mekinist).

L. Gastric, Esophageal and Esophagogastric Junction Cancer
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).

M. Hairy Cell Leukemia
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.

N. 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).

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when there is no evidence of unacceptable toxicity or disease progression or recurrence while on the current regimen. For patients using Tafinlar for adjuvant treatment of cutaneous melanoma, only 12 months of therapy total will be approved.

V. REFERENCES

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3. Micromedex Solutions [database online]. Ann Arbor, MI: Truven Health Analytics Inc. Updated periodically. www.micromedexsolutions.com [available with subscription]. Accessed November 15, 2023.
4. 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. 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.