Clinical Policy: Dabrafenib (Tafinlar)

Reference Number: CP.PHAR.239
Effective Date: 11.16.16
Last Review Date: 05.22
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Dabrafenib (Tafinlar®) is a kinase inhibitor.

FDA Approved Indication(s)

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
- In combination with trametinib (Mekinist®):
  - For the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test
  - 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
  - For the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with BRAF V600E mutation as detected by an FDA-approved test
  - For the treatment of patients with locally advanced or metastatic anaplastic thyroid cancer (ATC) with BRAF V600E mutation and with no satisfactory locoregional treatment options
  - For the treatment of adult and pediatric patients 6 years 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*

Limitation(s) 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.

** This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).*

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Tafinlar is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Melanoma (must meet all)**:**

1. Diagnosis of melanoma with BRAF V600E or V600K mutation;
2. Disease meets one of the following (a or b):
   a. Unresectable, limited resectable, or metastatic;
   b. Presence of lymph node(s) involvement following complete resection;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. Prescribed as one of the following (a or b):
   a. In combination with Mekinist;
   b. As a single agent for unresectable or metastatic disease with BRAF V600E mutation;
6. For Tafinlar requests, member must use generic dabrafenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. Request meets one of the following (a or b):*
   a. Dose does not exceed 300 mg (4 capsules) per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence)*.

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

B. Non-Small Cell Lung Cancer (must meet all)**:**

1. Diagnosis of advanced, metastatic, or recurrent NSCLC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is positive for a BRAF V600E mutation;
5. Prescribed in combination with Mekinist, unless the combination is not tolerated;
6. For Tafinlar requests, member must use generic dabrafenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. Request meets one of the following (a or b):*
   a. Dose does not exceed 300 mg (4 capsules) per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence)*.

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

C. Thyroid Cancer (must meet all)**:**

1. Diagnosis of advanced or metastatic thyroid cancer (ATC, follicular, papillary, or Hürthle cell carcinoma);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;

4. One of the following (a or b):
   a. For ATC: Disease is positive for BRAF V600E mutation;
   b. For follicular, papillary, or Hürthle cell carcinoma: both of the following (i and ii):
      i. Disease is positive for a BRAF mutation;
      ii. Disease is not amenable to radioactive iodine therapy;
5. For ATC requests, prescribed in combination with Mekinist;
6. For Tafinlar requests, member must use generic dabrafenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. Request meets one of the following (a or b):*
   a. Dose does not exceed 300 mg (4 capsules) per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence)*.

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

D. BRAF V600E Mutation-Positive Solid Tumor (must meet all):
1. Diagnosis of unresectable or metastatic solid tumor that is positive for a BRAF V600E mutation (*see Appendix D for examples*);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 6 years;
4. Disease has progressed on prior treatment, and no satisfactory alternative treatment options are available;
5. Prescribed in combination with Mekinist;
6. For Tafinlar requests, member must use generic dabrafenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. Request meets one of the following (a or b):
   a. Dose does not exceed one of the following (i, ii, or iii):
      i. Adults or pediatric patients weighing ≥ 51 kg: 300 mg (4 capsules) per day;
      ii. Pediatric patients weighing 26-37 kg: 150 mg (2 capsules) per day;
      iii. Pediatric patients weighing 38-50 kg: 200 mg (4 capsules) per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

E. Off-Label NCCN Compendium Recommended Indications (must meet all)**:**
1. Diagnosis of one of the following (a, b, or c):
   a. One of the following central nervous system cancers (i, ii, or iii):
      i. Adult low-grade (WHO Grade 1 or 2) glioma;
      ii. Recurrent anaplastic glioma;
      iii. Recurrent glioblastoma;

b. One of the following hepatobiliary cancers, as subsequent treatment in unresectable or metastatic disease (i, ii, or iii):
   i. Extrahepatic cholangiocarcinoma;
   ii. Gallbladder cancer;
   iii. Intrahepatic cholangiocarcinoma;
c. One of the following histiocytic neoplasms (i or ii):
   i. Erdheim-Chester Disease;
   ii. Langerhans Cell Histiocytosis;

2. Prescribed by or in consultation with one of the following (a or b):
   a. For central nervous system or hepatobiliary cancer: an oncologist;
   b. For histiocytic neoplasm: a hematologist or oncologist;
3. Age ≥ 18 years;
4. For central nervous system or hepatobiliary cancer: both of the following (a and b):
   a. Disease is positive for a BRAF V600E mutation;
   b. Prescribed in combination with Mekinist;
5. For histiocytic neoplasm: both of the following (a and b):
   a. Disease is positive for a BRAF V600E mutation;
   b. Tafinlar is prescribed as a single agent;
6. For Tafinlar requests, member must use generic dabrafenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. Request meets one of the following (a or b):*
   a. Dose does not exceed 300 mg (4 capsules) per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

F. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Tafinlar for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For Tafinlar requests, member must use generic dabrafenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed one of the following (i or ii):
      i. BRAF V600E mutation-positive solid tumor (1, 2, or 3):
         1) Adults or pediatric patients weighing ≥ 51 kg: 300 mg (4 capsules) per day;
         2) Pediatric patients weighing 26-37 kg: 150 mg (2 capsules) per day;
         3) Pediatric patients weighing 38-50 kg: 200 mg (4 capsules) per day;
      ii. All other indications: 300 mg (4 capsules) per day;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies –

CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ATC: anaplastic thyroid cancer
BRAF: B-Raf proto-oncogene, serine/ threonine kinase
FDA: Food and Drug Administration
NSCLC: non-small cell lung cancer

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: General Information

- Nearly half of patients with melanoma have a BRAF mutation gene. The most common forms of the BRAF mutation are V600E (80-90%) and V600K (10-20%).
- Tafinlar can potentiate the activity of the mitogen-activated protein kinases (MAPK) pathway in cells with wild-type BRAF and could accelerate the growth of some tumors with wild-type BRAF.
- Examples of solid tumors that may be BRAF V600E mutation-positive include, but are not limited to, the following: biliary tract cancer, high grade glioma (glioblastoma, anaplastic pleomorphic xanthoastrocytoma, anaplastic astrocytoma, astroblastoma, anaplastic ganglioglioma, and anaplastic oligodendroglioma), low grade glioma (astrocytoma, ganglioglioma, pleomorphic xanthoastrocytoma, pilocytic astrocytoma, choroid plexus papilloma, gangliocytoma/ganglioglioma), adenocarcinoma of small intestine, pancreas, or anus, mixed ductal/adenoneuroendocrine carcinoma, neuroendocrine carcinoma of colon, ameloblastoma of mandible, combined small cell-squamous carcinoma of lung, mucinous-papillary serous adenocarcinoma of peritoneum, gastrointestinal stromal tumor.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Melanoma, NSCLC, ATC	150 mg (two 75 mg capsules) PO BID The recommended duration of treatment in the adjuvant melanoma setting is until disease recurrence or unacceptable toxicity for up to 1 year. The recommended duration of treatment for all other indications is until disease progression or unacceptable toxicity.	300 mg/day
BRAF V600E mutation-positive	Adults: 150 mg (two 75 mg capsules) PO BID Pediatric patients: • 26-37 kg: 75 mg PO BID • 38-50 kg: 100 mg (two 50 mg capsules) PO BID	300 mg/day

Indication	Dosing Regimen	Maximum Dose
solid tumors	• ≥ 51 kg: 150 mg (two 75 mg capsules) PO BID The recommended duration of treatment is until disease progression or unacceptable toxicity.	

VI. Product Availability

Capsules: 50 mg, 75 mg

VII. References

1. Tafinlar Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; June 2022. Available at: https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/tafinlar.pdf. Accessed July 8, 2022.
2. Dabrafenib. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at NCCN.org. Accessed February 18, 2022.
3. National Comprehensive Cancer Network. Cutaneous Melanoma Version 2.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cutaneous_melanoma.pdf. Accessed February 18, 2022.
4. National Comprehensive Cancer Network. Central Nervous System Cancers Version 2.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf. Accessed February 18, 2022.
5. National Comprehensive Cancer Network Guidelines. Non-Small Cell Lung Cancer Version 1.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed February 18, 2022.
6. National Comprehensive Cancer Network Guidelines. Thyroid Carcinoma Version 3.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf. Accessed February 18, 2022.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2018 annual review: no significant changes; policies combined for Medicaid, Commercial, and HIM; added age; summarized NCCN and FDA approved uses for improved clarity; added specialist involvement in care and continuity of care statement; references reviewed and updated.	02.06.18	05.18
Updated criteria with new indications for anaplastic thyroid cancer and the adjuvant treatment of melanoma following complete lymph node(s) resection.	05.29.18	08.18
2Q 2019 annual review: no significant changes; references reviewed and updated.	02.26.19	05.19
2Q 2020 annual review: added NCCN supported off-label uses in colon and rectal cancers; added NCCN supported off-label dosing verbiage; for NSCLC added advanced disease; references reviewed and updated.	02.10.20	05.20

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2021 annual review: removed colorectal cancer off-label use as it is no longer included in the NCCN Compendium; oral oncology generic redirection language added; revised reference to HIM off-label use policy from HIM.PHAR.21 to HIM.PA.154; references reviewed and updated.	01.12.21	05.21
2Q 2022 annual review: Per NCCN added "limited resectable" melanoma classification, added allowance for therapy without Tafinlar for NSCLC, clarified thyroid cancer should be advanced or metastatic, clarified specific BRAF V600E mutation is a criterion for only ATC of thyroid cancers, added radioactive iodine therapy criterion for follicular, papillary, and Hürthle cell carcinomas, and added indications of central nervous system cancers, hepatobiliary cancers, and histiocytic neoplasms; Commercial approval duration revised from "Length of Benefit" to "12 months or duration of request, whichever is less"; references reviewed and updated.	02.21.22	05.22
RT4: revised criteria to include new FDA-approved indication of BRAF V600E mutation-positive solid tumors.	07.08.22	
Template changes applied to other diagnoses/indications and continued therapy section.	10.10.22	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to

applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.