

Clinical Policy Title:	dabrafenib
Policy Number:	RxA.526
Drug(s) Applied:	Tafinlar®
Original Policy Date:	03/06/2020
Last Review Date:	12/07/2021
Line of Business Policy Applies to:	All lines of business

Background

Dabrafenib (Tafinlar®) is a kinase inhibitor. It 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:
 - 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.

Limitation(s) of use: Tafinlar® is not indicated for treatment of patients with wild-type BRAF melanoma, wild-type BRAF NSCLC, or wild-type BRAF ATC.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
dabrafenib (Tafinlar®)	Melanoma, NSCLC, ATC	150 mg orally twice daily	300 mg/day

Dosage Forms

- Capsules: 50 mg, 75 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Melanoma (must meet all):

This clinical policy has been developed to authorize, modify, or determine coverage for individuals with similar conditions. Specific care and treatment may vary depending on individual need and benefits covered by the plan. This policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. This document may contain prescription brand name drugs that are trademarks of pharmaceutical manufacturers that are not affiliated with RxAdvance.

1. Diagnosis of melanoma with BRAF V600E or V600K mutation;
2. Disease meets one of the following (a or b):
 - a. Unresectable 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 a single agent for BRAF V600E mutation positive unresectable or metastatic melanoma;
6. Prescribed in combination with trametinib for following ;
 - a. BRAF V600E or V600K Mutation-Positive Unresectable or Metastatic Melanoma;
 - b. Adjuvant Treatment of BRAF V600E or V600K Mutation-Positive Melanoma
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: 6 months

Commercial: 6 months

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 trametinib;
6. 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: 6 months

Commercial: 6 months

C. Anaplastic Thyroid Cancer (ATC) (must meet all):

1. Diagnosis of ATC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is positive for BRAF V600E mutation;
5. Prescribed in combination with trametinib;
6. 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

Commercial: 6 months

Medicaid: 6 months

D. Central Nervous System Cancers (off label) (must meet all):

1. Diagnosis of advanced, metastatic or recurrent central nervous system cancers;
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 trametinib;
6. Prescribed as one of the following ways (a, b or b):
 - a. Adjuvant treatment of one of the following conditions (I, II, or III):
 - I. Pilocytic astrocytoma;
 - II. Pleomorphic xanthoastrocytoma;
 - III. Ganglioglioma;
 - b. Recurrent disease for one of the following conditions (I, II, or III):
 - I. Low-grade glioma;
 - II. Anaplastic glioma;
 - III. Glioblastoma;
 - c. Brain metastases from melanoma;
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: 6 months

Commercial: 6 months

E. Biliary Tract Cancers (off label) (must meet all):

1. Diagnosis of unresectable or metastatic Biliary Tract Cancers;
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 trametinib;
6. 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: 6 months

Commercial: 6 months

F. Histiocytic Neoplasms (off label) (must meet all):

1. Diagnosis of relapsed or refractory histiocytic neoplasms;
2. Disease meets one of the following (a or b):
 - a. Member has Langerhans cell histiocytosis with one of the following (a, b, or c):
 - I. Multisystem disease;
 - II. Pulmonary disease;
 - III. Central nervous system lesions;

- b. Member has Erdheim-Chester disease;
 3. Prescribed by or in consultation with an oncologist;
 4. Age ≥ 18 years;
 5. Disease is positive for a BRAF V600E mutation;
 6. 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: 6 months

Commercial: 6 months

G. Thyroid Carcinoma (off label) (must meet all):

1. Diagnosis of unresectable locoregional recurrent, persistent or distant metastases thyroid carcinoma;
 2. Prescribed by or in consultation with an oncologist;
 3. Age ≥ 18 years;
 4. Disease is positive for a progressive or symptomatic BRAF mutation;
 5. Disease is not susceptible to radioactive-iodine (RAI) therapy;
 6. Alternative systemic therapies are not available or appropriate;
 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: 6 months

Commercial: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or documentation supports that member is currently receiving Tafinlar® for the covered indication and has received this medication for at least 30 days;
 2. Member is responding positively to therapy;
 3. If request is for a dose increase, request meets one of the following (a or b):*
 - a. New dose does not exceed 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

Commercial: 6 months

Medicaid: 6 months

III. Appendices

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
MAPK: mitogen activated protein kinases
FDA: Food and Drug Administration

APPENDIX B: Therapeutic Alternatives

Not applicable.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
 - None reported.
- Boxed Warning(s):
 - 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.
- Tafinlar® is not FDA-approved to treat patients with V600K mutations. Studies with less than 20 patients showed a partial response rate ranging from 13 to 25 percent. Mekinist® is FDA-approved to treat V600K mutations.
- According to NCCN, Tafinlar® has category 2A recommendation for BRAF 600E mutation non-small lung cancer as a single agent or in combination with trametinib.
- According to NCCN, Tafinlar® has category 2A recommendation for combination treatment with Mekinist® for brain metastases if active against primary tumor (melanoma) for recurrent disease.

References

1. Tafinlar® Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; May 2021. Available at: <https://www.novartis.us/sites/www.novartis.us/files/tafinlar.pdf>. Accessed September 25, 2021.
2. Dabrafenib. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: https://www.nccn.org/professionals/drug_compendium/content/#. Accessed September 25, 2021.
3. National Comprehensive Cancer Network. Cutaneous Melanoma Version 2.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cutaneous_melanoma.pdf. Accessed September 25, 2021.
4. National Comprehensive Cancer Network Guidelines. Central Nervous System Cancers Version 2.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf. Updated September 11, 2020. Accessed September 25, 2021.
5. National Comprehensive Cancer Network Guidelines. Non-Small Cell Lung Cancer Version 5.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf Accessed September 25, 2021.
6. National Comprehensive Cancer Network Guidelines. Thyroid Carcinoma Version 2.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf Accessed September 25, 2021.
7. National Comprehensive Cancer Network Guidelines. Hepatobiliary Cancers Version 5.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf Accessed September 25, 2021.
8. National Comprehensive Cancer Network Guidelines. Histiocytic Neoplasms Version 2.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/histiocytic_neoplasms.pdf. Accessed September 25, 2021.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
<p>Policy was reviewed:</p> <ol style="list-style-type: none"> 1. Policy title table was updated. Line of business policy applies was updated to all lines of business 2. Initial approval criteria I.A.5 was updated to reflect current guideline prescribing methods. 3. Initial approval criteria I.B.5 was updated to reflect current guideline prescribing methods. 4. Updated brand name Mekinist® to generic trametinib in initial approval criteria. 5. Continued therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance...". 6. Commercial approval duration was updated from length of benefit to 6 months for initial and continued approval criteria. 7. References were updated. 	09/13/2020	12/07/2020
<p>Policy was reviewed:</p> <ol style="list-style-type: none"> 1. Statement about provider sample "The provision of provider samples does not guarantee coverage..." was added to Clinical Policy. 2. Initial Approval Criteria I.D was updated to include off label indication, "Central Nervous System Cancers." 3. Initial Approval Criteria I.E was updated to include off label indication, "Biliary Tract Cancers." 4. Initial Approval Criteria I.F was updated to include off label indication, "Histiocytic Neoplasms." 5. Initial Approval Criteria I.G was updated to include off label indication, "Thyroid Carcinoma." 6. Continued Therapy Approval II.A.1 was rephrased to "Member is currently receiving medication that has been 	09/25/2021	12/07/2021

<p>authorized by RxAdvance...".</p> <ol style="list-style-type: none">7. Initial and Continued Therapy Approval Criteria was updated to remove HIM approval duration..8. Appendix A was updated to include abbreviations for MAPK & FDA.9. References were reviewed and updated.		
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