Clinical Policy Title:	dabrafenib
Policy Number:	RxA.526
Drug(s) Applied:	Tafinlar®
Original Policy Date:	03/06/2020
Last Review Date:	08/28/2024
Line of Business Policy Applies to:	All lines of business (except Medicare)

Criteria

I. Initial Approval Criteria

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

1. Diagnosis of melanoma;
2. Prescribed as one of the following (a or b):
   a. As a single agent for unresectable or metastatic disease with BRAF V600E mutation;
   b. Used in combination with Mekinist (trametinib) or as adjuvant treatment for BRAF V600E or V600K mutations.

Approval Duration
All Lines of Business (except Medicare): 12 months

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

1. Diagnosis of recurrent, advanced, or metastatic NSCLC with BRAF V600E mutation;
2. Prescribed in combination with Mekinist (trametinib).

Approval Duration
All Lines of Business (except Medicare): 12 months

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

1. Diagnosis of locally advanced, unresectable, or metastatic ATC positive for BRAF V600E mutation;
2. Prescribed in combination with Mekinist (trametinib).

Approval Duration
All Lines of Business (except Medicare): 12 months

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;
2. Disease has progressed on prior treatment, and no satisfactory alternative treatment options are available;
3. Prescribed in combination with Mekinist (trametinib).

Approval Duration
All Lines of Business (except Medicare): 12 months

E. Pediatric Low-Grade Glioma (LGG) (must meet all)**:**

1. Diagnosis of LGG that is positive for a BRAF V600E mutation;
2. Prescribed in combination with Mekinist (trametinib).

Approval duration
All Lines of Business (except Medicare): 12 months

F. Central Nervous System Cancers (off-label) (must meet all)**:**
1. Diagnosis of central nervous system cancer with BRAF V600E positive mutation;
2. Prescribed In combination with Mekinist (trametinib);
3. Medication is being used for one of the following situations: (a, b or c):
   a. Adjuvant treatment of one of the following conditions (i, ii, or iii):
      i. Pilocytic astrocytoma;
      ii. Pleomorphic xanthoastrocytoma (PXA) (Grade 2); or;
      iii. Ganglioglioma;
   b. Recurrent disease for one of the following conditions (i, ii, or iii):
      i. Low-grade glioma;
      ii. Oliogdenroglioma
      iii. Isocitrate dehydrogenase-2 (IDH2)-mutant astrocytoma;
      iv. Glioblastoma;
   c. Brain metastases from melanoma.

Approval duration
All Lines of Business (except Medicare): 12 months

G. Hepatobiliary cancer (off label) (must meet all)**:**
1. Diagnosis of hepatobiliary cancer;
2. Member has progression on or after systemic treatment for unresectable or metastatic BRAF-V600E mutated biliary tract cancer like (a, b, or c):
   a. Gallbladder cancer;
   b. Extrahepatic cholangiocarcinoma;
   c. Intrahepatic cholangiocarcinoma;
3. Prescribed In combination with Mekinist (trametinib).

Approval duration
All Lines of Business (except Medicare): 12 months

H. Histiocytic Neoplasms (off label) (must meet all)**:**
1. Diagnosis of relapsed or refractory histiocytic neoplasms positive for a BRAF V600E mutation and meets one of the following (a or b):
   a. Member has Langerhans cell histiocytosis;
   b. Member has Erdheim-Chester disease;
2. Prescribed as a single agent.

Approval duration
All Lines of Business (except Medicare): 12 months

I. Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer (off-label) (must meet all)**:**
1. Diagnosis of persistent or low-grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer with BRAF V600E positive mutation;

2. Prescribed in combination with Mekinist (trametinib).

Approval duration
All Lines of Business (except Medicare): 12 months

J. Ampullary adenocarcinoma (off-label) (must meet all):
1. Diagnosis of ampullary adenocarcinoma and positive for a BRAF V600E mutation;
2. Prescribed in combination with Mekinist (trametinib).

Approval duration
All Lines of Business (except Medicare): 12 months

K. Esophageal and Esophagogastric Junction Cancers (off-label) (must meet all):
1. Diagnosis of esophageal or esophagogastric cancer and positive for a BRAF V600E mutation;
2. Prescribed in combination with Mekinist (trametinib).

Approval duration
All Lines of Business (except Medicare): 12 months

L. Gastric Cancer (off-label) (must meet all):
1. Diagnosis of gastric cancer;
2. Prescribed in combination with Mekinist (trametinib).

Approval duration
All Lines of Business (except Medicare): 12 months

M. Gastrointestinal Stromal Tumors (off-label) (must meet all):
1. Diagnosis of Gastrointestinal Stromal Tumors;
2. Prescribed in combination with Mekinist (trametinib).

Approval duration
All Lines of Business (except Medicare): 12 months

N. Neuroendocrine and Adrenal Tumors (off-label) (must meet all):
1. Diagnosis of Neuroendocrine and Adrenal Tumors and positive for BRAF V600E mutation;
2. Prescribed in combination with Mekinist (trametinib).

Approval duration
All Lines of Business (except Medicare): 12 months

O. Pancreatic Cancer (off-label) (must meet all):
1. Diagnosis of locally advanced or metastatic disease progression of pancreatic adenocarcinoma positive for BRAF V600E mutation;
2. Prescribed in combination with Mekinist (trametinib).

Approval duration
All Lines of Business (except Medicare): 12 months

P. Pediatric Central Nervous System (CNS) Cancers (off-label) (must meet all):
1. Member is positive for BRAF V600E mutation;
2. Used in combination with Mekinist (trametinib);

3. Member meets one of the following (a or b):
    a. Member has low grade glioma and requires systemic therapy;
    b. Member has diffuse high-grade gliomaand is using the requested medicationas adjuvant therapy.

Approval duration
All Lines of Business (except Medicare): 12 months

II. Continued Therapy Approval

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

1. Auto-approval based on lookback functionality within the past 120 days as a proxy for member responding positively to therapy.

Approval duration
All Lines of Business (except Medicare): 12 months

References

1. National Comprehensive Cancer Network. Cutaneous Melanoma Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cutaneous_melanoma.pdf. Accessed August 28, 2024.
2. National Comprehensive Cancer Network Guidelines. Central Nervous System Cancers Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf.Accessed August 28, 2024.
3. National Comprehensive Cancer Network Guidelines. Non-Small Cell Lung Cancer Version 8.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf Accessed August 28, 2024.
4. National Comprehensive Cancer Network Guidelines. Thyroid Carcinoma Version 4.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf Accessed August 28, 20243.
5. National Comprehensive Cancer Network Guidelines. Hepatobiliary Cancers Version 3.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf Accessed August 28, 2024.
6. National Comprehensive Cancer Network Guidelines. Histiocytic Neoplasms Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/histiocytic_neoplasms.pdf. Accessed August 28, 2024.
7. National Comprehensive Cancer Network Guidelines. Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer Version 3.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf . Accessed August 28, 2024.
8. National Comprehensive Cancer Network Guidelines. Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer Version 3.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf . Accessed August 28, 2024.
9. National Comprehensive Cancer Network Guidelines. Ampullary adenocarcinoma Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ampullary.pdf. Accessed August 28, 2024.
10. National Comprehensive Cancer Network Guidelines. Esophageal and Esophagogastric Junction Cancers Version 4.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/esophageal.pdf. Accessed August 28, 2024.
11. National Comprehensive Cancer Network Guidelines. Gastric Cancer Version 4.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf. Accessed August 28, 2024.
12. National Comprehensive Cancer Network Guidelines. Gastrointestinal Stromal Tumors Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/gist.pdf. Accessed August 28, 2024.
13. National Comprehensive Cancer Network Guidelines. Neuroendocrine and Adrenal Tumors Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf. Accessed August 28, 2024.
14. National Comprehensive Cancer Network Guidelines. Pancreatic Adenocarcinoma Version 3.2024. Available at:

https://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf. Accessed August 28, 2024.
15. National Comprehensive Cancer Network Guidelines. Pediatric Central Nervous System Cancers Version 1.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ped_cns.pdf. Accessed August 28, 2024.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 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
Policy was reviewed: 1. Initial Approval Criteria I.D was updated to include off label indication, "Central Nervous System Cancers." 2. Initial Approval Criteria I.E was updated to include off label indication, "Biliary Tract Cancers." 3. Initial Approval Criteria I.F was updated to include off label indication, "Histiocytic Neoplasms." 4. Initial Approval Criteria I.G was updated to include off label indication, "Thyroid Carcinoma." 5. Continued Therapy Approval II.A.1 was	09/25/2021	12/07/2021

rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 6. Initial and Continued Therapy Approval Criteria was updated to remove HIM approval duration.. 7. References were reviewed and updated.		
Policy was reviewed: 1. Initial Approval Criteria, I.A.5 and I.A.6: Updated prescriber criteria from Prescribed as a single agent for BRAF V600E mutation positive unresectable or metastatic melanoma; Prescribed in combination with trametinib for following; BRAF V600E or V600K Mutation-Positive Unresectable or Metastatic Melanoma; Adjuvant Treatment of BRAF V600E or V600K Mutation-Positive Melanoma to 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; 2. Initial Approval Criteria, I.C.: Merged Thyroid cancer and ATC in a single criteria. 3. Initial Approval Criteria, I.G: Updated to include approval criteria for indication, BRAF V600E Mutation-Positive Solid Tumor. 4. Initial Approval Criteria, I.G: Updated to include approval criteria for indication, Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer 5. Continued Therapy Approval Crtieria, II.A.3: Updated to include dosing criteria for BRAF V600E Mutation-Positive Solid Tumor. 6. References were reviewed and updated.	09/13/2022	10/19/2022

Policy was reviewed: 1. Initial Approval Criteria, I.A.1: Updated diagnosis criteria from Diagnosis of melanoma with BRAF V600E or V600K mutation to Diagnosis of melanoma. 2. Initial Approval Criteria, I.A.2: Updated to remove prior diagnostic criteria "Disease meets one of the following (a or b): a. Unresectable or metastatic; b. Presence of lymph node(s) involvement following complete resection;". 3. Initial Approval Criteria, I.A.4.b: Updated precribing criteria from In combination with Mekinist to Used in combination with Mekinist (trametinib) or as adjuvant treatment for BRAF V600E or V600K mutations. 4. Initial Approval Criteria, I.B.1: Updated dosing criteria from Diagnosis of advanced, metastatic or recurrent NSCLC to Diagnosis of recurrent, advanced, or metastatic NSCLC with BRAF V600E mutation. 5. Initial Approval Criteria, I.B.4: Updated prescribing criteria from Prescribed in combination with trametinib to Prescribed in combination with Mekinist (trametinib). 6. Initial Approval Criteria, I.B.4: Updated to remove prior diagnostic criteria "Disease is positive for a BRAF V600E mutation". 7. Initial Approval Criteria, I.C.1: Updated diagnostic criteria from Diagnosis of thyroid Cancer (ATC, follicular, papillary, or Hürthle cell carcinoma) to Diagnosis of locally advanced, unresectable, or metastatic ATC positive for BRAF V600E mutation. 8. Initial Approval Criteria, I.C.4: Updated prescribing criteria from Prescribed in	06/06/2023	07/13/2023

combination with trametinib to Prescribed in combination with Mekinist (trametinib). 9. Initial Approval Criteria, I.C.4: Updated to remove prior diagnostic criteria "Disease is positive for a BRAF V600E mutation". 10. Initial Approval Criteria, I.C.6: Updated to remove prior meeting criteria "Member meets 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;". 11. Initial Approval Criteria, I.C.7: Updated to remove prior prescribing criteria "For ATC requests, prescribed in combination with Mekinist®". 12. Initial Approval Criteria, I.E: Updated to include approval criteria for indication, Pediatric Low-Grade Glioma. 13. Initial Approval Criteria, I.F.1: Updated diagnosis criteria from Diagnosis of advanced, metastatic or recurrent central nervous system cancers to Diagnosis of central nervous system cancer with BRAF V600E positive mutation. 14. Initial Approval Criteria, I.F.4: Updated to remove prior diagnostic criteria "Disease is positive for a BRAF V600E mutation". 15. Initial Approval Criteria, I.F.5: Updated criteria from Prescribed as one of the following ways to Medication is being used for one (1) of the following situations. 16. Initial Approval Criteria, I.F.5.b.ii: Updated to remove prior criteria pertaining to		

indication Central Nervous System Cancers (off-label), "Anaplastic glioma". 17. Initial Approval Criteria, I.F.5.b.ii and I.F.5.b.iii: Updated to add criteria pertaining to indication Central Nervous System Cancers (off-label), Oliogdenroglioma and Isocitrate dehydrogenase-2 (IDH2)-mutant astrocytoma. 18. Initial Approval Criteria, I.G.1: Update diagnosis criteria from Diagnosis of one of the hepatobiliary cancers, as subsequent treatment in unresectable or metastatic disease (a, b, or c); a. Extrahepatic cholangiocarcinoma; b. Gallbladder cancer; c. Intrahepatic cholangiocarcinoma to Diagnosis of hepatobiliary cancer. 19. Initial Approval Criteria, I.G.2:Updated to include new diagnostic criteria Member has progression on or after systemic treatment for unresectable or metastatic BRAF-V600E mutated biliary tract cancer like (a, b, or c): a. Gallbladder cancer; b. Extrahepatic cholangiocarcinoma; c. Intrahepatic cholangiocarcinoma. 20. Initial Approval Criteria, I.G.5: Updated prescribing criteria from Prescribed in combination with trametinib to Prescribed in combination with Mekinist (trametinib). 21. Initial Approval Criteria, I.H.1: Update diagnosis criteria from Diagnosis of relapsed or refractory histiocytic neoplasms to Diagnosis of relapsed or refractory histiocytic neoplasms positive for a BRAF V600E mutation and meets one of the following (a or b): a. Member has Langerhans cell histiocytosis;		

b. Member has Erdheim-Chester disease; 22. Initial Approval Criteria, I.H.2: Update to remove prior disease meeting criteria "Disease meets one of the following (a or b): a. Member has Langerhans cell histiocytosis with one of the following (i, ii or iii): i. Multisystem disease; ii. Pulmonary disease; iii. Central nervous system lesions; b. Member has Erdheim-Chester disease;". 23. Initial Approval Criteria, I.H.5: Updated to remove prior diagnostic criteria "Disease is positive for a BRAF V600E mutation". 24. Initial Approval Criteria, I.I.1: Updated diagnosis criteria from Diagnosis of Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer with persistence or recurrence in BRAF V600E positive tumors to Diagnosis of persistent or low-grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer with BRAF V600E positive mutation. 25. Initial Approval Criteria, I.I.4: Updated to remove prior member meets criteria "Member meets any one of the followings (a, b, c or d): a. Disease progression on primary, maintenance, or recurrence therapy (platinum-resistant disease); b. For stable or persistent disease (if not on maintenance therapy) (platinum-resistant disease); c. For complete remission and relapse <6 months after completing chemotherapy (platinumresistant disease);		

d. For radiographic and/or clinical relapse in patients with previous complete remission and relapse ≥ 6 months after completing prior chemotherapy (platinum-sensitive disease);". 26. Initial Approval Criteria, I.I.6: Updated to remove prior diagnostic criteria "Disease is positive for a BRAF V600E mutation". 27. Initial Approval Criteria, I.A, I.B, I.C, I.D, I.E, I.F, I.G, I.H, I.I: Updated approval duration criteria from 12 months to 6 months for both Commercial and Medicaid. 28. Initial Approval Criteria, I.J: Updated to include approval criteria for indication, Ampullary adenocarcinoma. 29. Initial Approval Criteria, I.K: Updated to include approval criteria for indication, Esophageal and Esophagogastric Junction Cancers. 30. Initial Approval Criteria, I.L: Updated to include approval criteria for indication, Gastric Cancer. 31. Initial Approval Criteria, I.M: Updated to include approval criteria for indication, Gastrointestinal Stromal Tumors . 32. Initial Approval Criteria, I.N: Updated to include approval criteria for indication, Neuroendocrine and Adrenal Tumors. 33. Initial Approval Criteria, I.O: Updated to include approval criteria for indication, Pancreatic Cancer. 34. Initial Approval Criteria, I.P: Updated to include approval criteria for indication, Pediatric Central Nervous System (CNS) Cancers. 35. Continued Therapy Approval Criteria, II.A.1: Updated documentation criteria from 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 to 1. Member is currently receiving medication that has been authorized by RxAdvance or member has met initial approval criteria listed in this policy. 36. Continued Therapy Approval Criteria, II.A: Updated approval duration criteria from 6 months to 12 months for both Commercial and Medicaid. 37. References were reviewed and updated.		
Policy was reviewed.	10/19/2023	10/19/2023
Policy was reviewed: 1. Removed age restrictions. 2. Removed prescriber restrictions. 3. Removed dose restrictions. 4. Updated Continued therapy approval with auto-approval based on lookback functionality within the past 120 days. 5. Removed reauthorization requirement for positive response to therapy. 6. Updated approval duration verbiage. 7. References were reviewed and updated.	8/28/2024	9/13/2024