Reference number(s)
1681-A

SPECIALTY GUIDELINE MANAGEMENT

MEKINIST (trametinib)

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. Mekinist is indicated, as a single agent or in combination with dabrafenib, for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test.
2. Mekinist is indicated, in combination with dabrafenib, for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with BRAF V600E mutation as detected by an FDA-approved test.
3. Mekinist is indicated, in combination with dabrafenib, 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. Mekinist is indicated, in combination with dabrafenib, for the treatment of patients with locally advanced or metastatic anaplastic thyroid cancer (ATC) with BRAF V600E mutation and no satisfactory locoregional treatment options.

B. Compendial Uses
1. Melanoma (including brain metastases), BRAF V600 activating mutation-positive
2. Glioma, BRAF V600 activating mutation-positive
3. Meningioma, BRAF V600 activating mutation-positive
4. Astrocytoma, BRAF V600 activating mutation-positive
5. Uveal melanoma as a single agent
6. Brain cancer and neurofibromatosis type 1
7. Low grade serous ovarian carcinoma

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of BRAF mutation documentation is necessary to initiate the prior authorization review for applicable indications as outlined in section III.

III. CRITERIA FOR INITIAL APPROVAL

A. Melanoma

Authorization of 12 months may be granted for treatment of melanoma in any of the following settings:
1. Unresectable or metastatic cutaneous melanoma with a BRAF V600 activating mutation as a single agent or in combination with dabrafenib (Tafinlar).

© 2021 CVS Caremark. All rights reserved.

This document contains confidential and proprietary information of CVS Caremark and cannot be reproduced, distributed or printed without written permission from CVS Caremark. This document contains prescription brand name drugs that are trademarks or registered trademarks of pharmaceutical manufacturers that are not affiliated with CVS Caremark.

2. Brain metastases from melanoma with a BRAF V600 activating mutation in combination with dabrafenib (Tafinlar).
3. Adjuvant treatment of stage III cutaneous melanoma with a BRAF V600 activating mutation in combination with dabrafenib (Tafinlar) following complete resection or no evidence of disease.
4. Uveal melanoma as a single agent for distant metastatic disease.

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 in combination with dabrafenib (Tafinlar).

C. Anaplastic Thyroid Cancer (ATC)
Authorization of 12 months may be granted for treatment of metastatic BRAF V600E mutation-positive ATC in combination with dabrafenib (Tafinlar).

D. Central Nervous System Cancer
Authorization of 12 months may be granted for treatment of central nervous system cancer in a member with either of the following:
1. BRAF V600 mutation-positive gliomas, meningiomas, or astrocytomas
2. Brain cancer and neurofibromatosis type 1

E. Low Grade Serous Ovarian Carcinoma
Authorization of 12 months may be granted for treatment of persistent disease or recurrence of low-grade serous ovarian carcinoma.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen. For patients using Mekinist for adjuvant treatment of cutaneous melanoma, only 12 months of therapy total will be approved.

V. REFERENCES

1. Mekinist [package insert]. East Hanover, NJ: Novartis Pharmaceutical Corporation; June 2020.
2. The NCCN Drugs & Biologics Compendium 2020 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed November 10, 2020.
3. 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. *J Neuropathol Exp Neurol.* 2015;74(10):960-969. doi:10.1097/NEN.0000000000000240.
4. 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. *Pediatr Hematol Oncol*. 2015; 32:3, 207-211, DOI: 10.3109/08880018.2014.936058
5. 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.
6. 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. *J Natl Compr Canc Netw.* 2016;14(11):1345-1350.
7. Knight T, Shatara M, Carvalho L, et al. Dramatic response to trametinib in a male child with neurofibromatosis type 1 and refractory astrocytoma. *Pediatr Blood Cancer*. 2019; 66(1):e27474.

© 2021 CVS Caremark. All rights reserved.

This document contains confidential and proprietary information of CVS Caremark and cannot be reproduced, distributed or printed without written permission from CVS Caremark. This document contains prescription brand name drugs that are trademarks or registered trademarks of pharmaceutical manufacturers that are not affiliated with CVS Caremark.

8. See WL, Tan IL, Mukherjee J, et al. Sensitivity of Glioblastomas to Clinically Available MEK Inhibitors Is Defined by Neurofibromin 1 Deficiency. *Cancer Res*. 2012;72(13):3350.

© 2021 CVS Caremark. All rights reserved.

This document contains confidential and proprietary information of CVS Caremark and cannot be reproduced, distributed or printed without written permission from CVS Caremark. This document contains prescription brand name drugs that are trademarks or registered trademarks of pharmaceutical manufacturers that are not affiliated with CVS Caremark.