Commercial/Healthcare Exchange PA Criteria
Effective: November 2, 2016

Prior Authorization: Mekinist

Products Affected: Mekinist (trametinib) oral tablet

Medication Description:

Mekinist is a kinase inhibitor indicated as a single agent or in combination with Taflinar (dabrafenib) for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by a Food and Drug Administration (FDA)-approved test. Mekinist as a single agent is not indicated for the treatment of patients who have received prior BRAF-inhibitor therapy.

Mekinist is a reversible inhibitor of mitogen-activated extracellular signal-regulated kinase 1 (MEK1) and MEK2 activation and of MEK1 and MEK2 kinase activity. MEK proteins are upstream regulators of the extracellular signal-related kinase (ERK) pathway, which promotes cellular proliferation. BRAF V600E mutations result in constitutive activation of the BRAF pathway, which includes MEK1 and MEK2. Mekinist inhibits BRAF V600 mutation-positive melanoma cell growth *in vitro* and *in vivo*.

Mekinist and Tafinlar target two different kinases in the RAS/RAF/MEK/ERK pathway. Use of Mekinist and Tafinlar in combination resulted in greater growth inhibition of BRAF V600 mutation-positive melanoma cell lines *in vitro* and prolonged inhibition of tumor growth in BRAF V600 mutation positive melanoma xenografts compared with either drug alone.

Covered Uses:

1. BRAF V600E or V600K Mutation-Positive Unresectable or Metastatic Melanoma
2. Adjuvant Treatment of BRAF V600E or V600K Mutation-Positive Melanoma
3. BRAF V600E Mutation-Positive Metastatic NSCLC
4. BRAF V600E Mutation-Positive Locally Advanced or Metastatic Anaplastic Thyroid Cancer

Exclusion Criteria:

Mekinist has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval in the following circumstances:

1. In patients with melanoma who have progressed on prior BRAF inhibitor therapy.
2. In patients with mutations other than BRAF V600E or BRAF V600K.

Required Medical Information:

1. Diagnosis
2. BRAF mutation status
3. Previous therapies tried
4. Dose and frequency

Age Restrictions: None.

Prescriber Restrictions: None.

Coverage Duration:

Initial: 12 months
Continuation: 3 years

Other Criteria:

1. **Melanoma, Unresectable or Metastatic.** Approve if the patient meets the following criteria (i, ii, and iii):
   i. The patient has a diagnosis of melanoma that is metastatic or unresectable; AND
   ii. The patient has documented BRAF V600E or V600K mutations; AND
   iii. The patient meets ONE of the following conditions (a or b):
      a. Mekinist will be used in combination with Tafinlar; OR
      b. Mekinist will be used as monotherapy in a patient who has not previously experienced disease progression on prior BRAF inhibitor therapy (e.g., Tafinlar or Zelboraf [vemurafenib]).
2. **Adjuvant Treatment of BRAF V600E or V600K Mutation-Positive Melanoma. Approve if the patient meets the following criteria:**
   a. Mekinist will be used as adjuvant treatment
   b. The patient has a diagnosis of melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test
   c. The patients diagnosis includes the involvement of lymph nodes, following complete resection

3. **BRAF V600E Mutation-Positive Metastatic NSCLC. Approve if the patient meets the following criteria:**
   a. The patient has a diagnosis of metastatic non-small cell lung cancer (NSCLC) with BRAF V600E mutation as detected by an FDA-approved test; AND
   b. Mekinist will be used in combination with dabrafenib

4. **BRAF V600E Mutation-Positive Locally Advanced or Metastatic Anaplastic Thyroid Cancer. Approve if the patient meets the following criteria:**
   a. The patient has a diagnosis of locally advanced or metastatic anaplastic thyroid cancer (ATC) with BRAF V600E mutation and with no satisfactory locoregional treatment options; AND
   b. Mekinist will be used in combination with dabrafenib

References:

1. Mekinist [prescribing information]. New York, NY: Novartis Pharmaceuticals Corporation; August 2016.
2. The NCCN Clinical Practice Guidelines in Oncology: Melanoma (Version 3.2016). © 2015 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on August 9, 2016

Policy Revision history

Rev #	Type of Change	Summary of Change	Sections Affected	Date

1	New Policy	New Policy	All	8/15/16
2	Update	Criteria changed to match Updated FDA Label CCI Adopted EH criteria, removed from “Oncology Policy”	Covered Uses Exclusion Criteria Other Criteria	3/7/19
3	Update	Added continuation coverage duration of 3 years	Coverage Duration	7/1/2019