Mekinist

Description

Mekinist (trametinib)

Background
Mekinist is used, as a single agent or in combination with Tafinlar (dabrafenib), for the treatment of advanced melanoma that is unresectable (cannot be removed by surgery) or metastatic (late-stage) that express the BRAF V600E or V600K gene mutations. Mekinist can also be used for resectable melanoma (can also be considered stage III or locally advanced) in combination with dabrafenib, for the adjuvant treatment of patients with melanoma with BRAF V600E or V600K mutations following complete resection. Additionally, Mekinist in combination with dabrafenib is used to treat patients with metastatic non-small cell lung cancer (NSCLC) with BRAF V600E mutation, as well as in patients with locally advanced or metastatic anaplastic thyroid cancer with no satisfactory locoregional treatment options. Approximately half of melanomas have a BRAF gene mutation. A companion diagnostic genetic test called the THxID BRAF test will determine if a patient’s melanoma cells have the specific V600E or V600K mutation in the BRAF gene (1-4).

Mekinist and Tafinlar, when combined, are used to block signaling in different sites of the same molecular pathway that promotes cancer cell growth. They are specifically indicated as a combination therapy for patients with melanoma whose tumors express gene mutations called BRAF V600E and V600K. The BRAF protein is involved in the regulation of normal cell growth, but it is mutated in approximately half of melanomas arising from the skin (1-4).

Regulatory Status
FDA-approved indication: Mekinist is a kinase inhibitor indicated as: (1)
1. Single agent for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test.
2. Combination treatment with dabrafenib (Tafinlar) for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test.
3. Combination treatment with dabrafenib (Tafinlar) 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. Combination treatment with dabrafenib (Tafinlar) for the treatment of patients with locally advanced or metastatic anaplastic thyroid cancer with no satisfactory locoregional treatment options.
5. Combination treatment with dabrafenib (Tafinlar) for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with BRAF V600E mutation as detected by an FDA-approved test.

Limitation of use:
Mekinist is not indicated for the treatment of patients who have received prior BRAF inhibitor therapy (1).

Off-Label Uses: (2-4)
1. Second line treatment or subsequent therapy for unresectable or metastatic melanoma
2. Non-Small Cell Lung Cancer (NSCLC)

Prior to initiation of therapy, the presence of BRAF V600E or V600K mutation in tumor specimens must be confirmed (1).

Hemorrhages, including major hemorrhages defined as symptomatic bleeding in a critical area or organ can occur in patients receiving Mekinist in combination with dabrafenib (Tafinlar). Permanently discontinue Mekinist, and also permanently discontinue dabrafenib if administered in combination, for all Grade 4 hemorrhagic events and for any Grade 3 hemorrhagic events that do not improve. Withhold Mekinist for up to 3 weeks for Grade 3 hemorrhagic events; if improved resume at a lower dose level. Withhold dabrafenib for Grade 3 hemorrhagic events; if improved resume at a lower dose level (1).

Venous thromboembolism, such as deep vein thrombosis and pulmonary embolism, can occur in patients receiving Mekinist in combination with dabrafenib (1).
Mekinist has a risk of developing cardiomyopathy defined as cardiac failure, left ventricular dysfunction, or decreased left ventricular ejection fraction (LVEF). Before initiation of Mekinist, assess LVEF by echocardiogram or multigated acquisition (MUGA) scan, one month after initiation of Mekinist, and then every 2 to 3 months during treatment. Withhold treatment if absolute LVEF value decreases by 10% from pre-treatment values and is less than the lower limit of normal. Permanently discontinue Mekinist for symptomatic cardiomyopathy or persistent, asymptomatic LVEF dysfunction that does not resolve within 4 weeks (1).

Mekinist can cause severe visual problems including retinal pigment epithelial detachment (RPED) and retinal vein occlusion (RVO). A physician should perform an eye exam at any time a patient reports visual disturbances and compare to baseline, if available. Withhold Mekinist if RPED is diagnosed. If resolution of the RPED is documented on repeat eye exam within 3 weeks, resume Mekinist at a reduced dose. If a patient reports loss of vision or other visual disturbances, perform eye exam within 24 hours (1).

Mekinist treatment must be withheld for new or progressive unexplained pulmonary symptoms or findings, such as cough, dyspnea, hypoxia, or infiltrates. Mekinist must be permanently discontinued for patients diagnosed with treatment-related interstitial lung disease (ILD) or pneumonitis (1).

There is a potential risk of skin toxicity while taking Mekinist. Skin toxicity includes rash, dermatitis, acneiform rash, palmar-plantar erythrodysesthesia syndrome, and erythema. Patients must be monitored for skin toxicities and for secondary infections while taking Mekinist with a dose adjustment or discontinued based on the severity of the adverse reaction (1). Mekinist can cause embryofetal toxicity and impaired fertility. Advise female patients of reproductive potential to use highly effective contraception during treatment and for 4 months after treatment (1).

The safety and effectiveness of Mekinist have not been established in pediatric patients (1).

**Related Policies**
Braftovi, Cotellic, Mektovi, Tafinlar, Zelboraf

**Policy**
This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.
Mekinist may be considered **medically necessary** in patients 18 years of age or older for unresectable or metastatic melanoma, for resectable melanoma, for non-small cell lung cancer (NSCLC), or for locally advanced or metastatic anaplastic thyroid cancer (ATC), and if the conditions indicated below are met.

Mekinist is considered **investigational** in patients less than 18 years of age and for all other indications.

**Prior-Approval Requirements**

**Age**  
18 years of age and older

**Diagnoses**

Patient must have **ONE** of the following:

1. Unresectable or metastatic melanoma

   **AND ONE** of the following:
   a. Used as a single agent with documented BRAF V600E or BRAF V600K mutations as detected by an FDA-approved test
   b. Used in combination with dabrafenib (Tafinlar) with documented BRAF V600E or BRAF V600K mutation as detected by an FDA-approved test

2. Resectable melanoma
   a. Used in combination with dabrafenib (Tafinlar) with documented BRAF V600E or BRAF V600K mutation as detected by an FDA-approved test
   b. Melanoma has lymph node involvement
   c. Used as adjuvant treatment after complete resection

3. Non-Small Cell Lung Cancer (NSCLC)
   a. Used in combination with dabrafenib (Tafinlar) with documented BRAF V600E mutation as detected by an FDA-approved test

4. Locally advanced or metastatic anaplastic thyroid cancer (ATC)
   a. Used in combination with dabrafenib (Tafinlar) with documented BRAF V600E mutation as detected by an FDA-approved test
Prior – Approval **Renewal Requirements**

**Age** 18 years of age and older

**Diagnoses**

Patient must have **ONE** of the following:

1. Unresectable or metastatic melanoma

   **AND ONE** of the following:
   
   a. Used as a single agent with documented BRAF V600E or BRAF V600K mutations as detected by an FDA-approved test
   
   b. Used in combination with dabrafenib (Tafinlar) with documented BRAF V600E or BRAF V600K mutation as detected by an FDA-approved test

2. Non-Small Cell Lung Cancer (NSCLC)

   a. Used in combination with dabrafenib (Tafinlar) with documented BRAF V600E mutation as detected by an FDA-approved test

3. Locally advanced or metastatic anaplastic thyroid cancer (ATC)

   a. Used in combination with dabrafenib (Tafinlar) with documented BRAF V600E mutation as detected by an FDA-approved test

   **AND** the following:
   
   a. Absence of disease progression

**Policy Guidelines**

**Pre - PA Allowance**

None

**Prior - Approval Limits**
**Quantity**

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<tr>
<th>Strength</th>
<th>Quantity per 90 days</th>
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<tbody>
<tr>
<td>0.5 mg</td>
<td>360 tablets per 90 days OR</td>
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<tr>
<td>2 mg</td>
<td>90 tablets per 90 days</td>
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**Duration**

12 months

**Prior – Approval Renewal Limits**

Same as above

No renewal for resectable melanoma diagnosis

**Rationale**

**Summary**

Mekinist is approved for patients 18 years of age or older for unresectable or metastatic melanoma with BRAF V600E or V600K mutation, confirmed by an FDA-approved test. Mekinist can also be used for resectable melanoma (can also be considered stage III or locally advanced) in combination with dabrafenib, for the adjuvant treatment of patients with melanoma with BRAF V600E or V600K mutations following complete resection. Additionally, Mekinist in combination with dabrafenib is used to treat patients with metastatic non-small cell lung cancer (NSCLC) with BRAF V600E mutation as well as patients with locally advanced or metastatic anaplastic thyroid cancer with no satisfactory locoregional treatment options. Mekinist can cause multiple severe visual problems including retinal pigment epithelial detachment (RPED) and retinal vein occlusion (RVO). Mekinist treatment may cause interstitial lung disease or pneumonitis. There is a potential risk of skin toxicity while taking Mekinist. Mekinist can cause embryofetal toxicity and impaired fertility. The safety and effectiveness of Mekinist have not been established in pediatric patients (1-4).

Prior authorization is required to ensure the safe, clinically appropriate and cost-effective use of Mekinist while maintaining optimal therapeutic outcomes.

**References**


### Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
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<tbody>
<tr>
<td>June 2013</td>
<td>New Policy</td>
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<tr>
<td>September 2013</td>
<td>Annual editorial and reference update.</td>
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<tr>
<td></td>
<td>Addition to criteria to allow combination therapy with Tafinlar.</td>
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<tr>
<td>February 2014</td>
<td>Aligned criteria to new package insert.</td>
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<tr>
<td></td>
<td>Revised the requirement that the patient must have NO prior BRAF therapy pertains to Mekinist used as a single agent only.</td>
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<td>Addition of new warnings and precautions with the combined therapy: new malignancies, hemorrhages, and venous thromboembolism.</td>
</tr>
<tr>
<td>September 2014</td>
<td>Annual editorial and reference update</td>
</tr>
<tr>
<td>December 2014</td>
<td>Annual editorial and reference update</td>
</tr>
<tr>
<td></td>
<td>Removal of warnings and precautions: Assess left ventricular ejection fraction (LVEF), absence of symptomatic congestive heart failure, interstitial lung disease (ILD), retinal vein occlusion</td>
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<tr>
<td>June 2015</td>
<td>Annual review</td>
</tr>
<tr>
<td>March 2016</td>
<td>Annual editorial review and reference update</td>
</tr>
<tr>
<td></td>
<td>Policy number change from 5.04.38 to 5.21.38</td>
</tr>
<tr>
<td>June 2016</td>
<td>Annual editorial review and reference update</td>
</tr>
<tr>
<td></td>
<td>Addition of Non-Small Cell Lung Cancer (NSCLC)</td>
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<tr>
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<td>Removal of the requirement: if Mekinist is used as a single agent only that the patient must have NO prior BRAF inhibitor treatment.</td>
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<tr>
<td>June 2017</td>
<td>Annual editorial review and reference update</td>
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<tr>
<td>June 2018</td>
<td>Annual review and reference update</td>
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<tr>
<td></td>
<td>Addition of the diagnoses of resectable melanoma and locally advanced or metastatic anaplastic thyroid cancer to criteria</td>
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<tr>
<td></td>
<td>Addition of quantity limits to criteria and combination with Tafinlar requirements in renewal section</td>
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<tr>
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This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 20, 2019 and is effective July 1, 2019.