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5.21.038

Section:	Prescription Drugs	**Effective Date:**	January 1, 2024
Subsection:	Antineoplastic Agents	**Original Policy Date:**	June 19, 2013
Subject:	Mekinist	**Page:**	1 of 8

Last Review Date: December 8, 2023

Mekinist

Description

Mekinist (trametinib)

Background
Mekinist (trametinib) 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 cell growth of various BRAF V600 mutation-positive tumors. Mekinist and dabrafenib (Tafinlar) target two different kinases in the RAS/RAF/MEK/ERK pathway. Use of these agents together results in greater growth inhibition of BRAF V600 mutation-positive tumor cell lines (1).

Regulatory Status
FDA-approved indications: Mekinist is a kinase inhibitor indicated: (1)

1. As a single agent for the treatment of BRAF-inhibitor treatment-naïve patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test.
2. In combination 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. In combination 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. In combination 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.
5. In combination with dabrafenib (Tafinlar) for the treatment of patients with locally advanced or metastatic anaplastic thyroid cancer (ATC) with no satisfactory locoregional treatment options.
6. In combination with dabrafenib (Tafinlar) for the treatment of adult and pediatric patients 1 year of age and older with unresectable or metastatic solid tumors with BRAF V600E mutation who have progressed following prior treatment and have no satisfactory alternative treatment options.
7. In combination with dabrafenib (Tafinlar) for the treatment of pediatric patients 1 year of age and older with low-grade glioma (LGG) with a BRAF V600E mutation who require systemic therapy.

Limitations of Use: (1)
Mekinist is not indicated for the treatment of patients with colorectal cancer because of known intrinsic resistance to BRAF inhibition.

Off-Label Uses: (2-3)
1. Low-grade serous ovarian cancer

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. Permanently discontinue Mekinist 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 the next lower dose level (1).

Venous thromboembolism, such as deep vein thrombosis and pulmonary embolism, can occur in patients receiving Mekinist (1).

Mekinist has a risk of developing cardiomyopathy. AAssess left ventricular ejection fraction (LVEF) by echocardiogram or multigated acquisition (MUGA) scan before initiation of Mekinist, one month after initiation of Mekinist, and then every 2 to 3 months during treatment (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 periodically and at any time a patient reports visual disturbances and compare to baseline, if available. Withhold Mekinist if RPED is diagnosed. Permanently discontinue Mekinist in patients with documented RVO. 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 and findings, such as cough, dyspnea, hypoxia, pleural effusion, 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. Patients should be monitored for new or worsening serious skin reactions (1).

Mekinist can cause embryo-fetal toxicity and impaired fertility. Advise female patients of reproductive potential to use effective contraception during treatment with Mekinist and for 4 months after treatment (1).

The safety and effectiveness of Mekinist in combination with dabrafenib (Tafinlar) have not been established in pediatric patients less than 1 year old with unresectable or metastatic solid tumors and with LGG. The safety and effectiveness of Mekinist for all other indications in pediatric patients have not been established (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** if the conditions indicated below are met.

Mekinist may be considered **investigational** for all other indications.

Prior-Approval Requirements

Diagnoses

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

1. Unresectable or metastatic melanoma
    a. 18 years of age or older
    b. Patient has **ONE** of the following:
        i. Used as a single agent with documented BRAF V600E or BRAF V600K mutations as detected by an FDA-approved test
        ii. 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. 18 years of age or older
    b. Used in combination with dabrafenib (Tafinlar) with documented BRAF V600E or BRAF V600K mutation as detected by an FDA-approved test
    c. Melanoma has lymph node involvement
    d. Used as adjuvant treatment after complete resection

3. Metastatic non-small cell lung cancer (NSCLC)
    a. 18 years of age or older
    b. 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. 18 years of age or older
    b. Used in combination with dabrafenib (Tafinlar) with documented BRAF V600E mutation
    c. **NO** satisfactory locoregional treatment options

5. Unresectable or metastatic solid tumors
    a. 1 year of age or older
    b. Used in combination with dabrafenib (Tafinlar) with documented BRAF V600E mutation
    c. Patient has progressed following prior treatment
    d. **NO** satisfactory alternative treatment options

6. Low-grade glioma (LGG)
    a. 1 year of age or older
    a. Used in combination with dabrafenib (Tafinlar) with documented BRAF V600E mutation
    b. Patient requires systemic therapy

7. Low-grade serous ovarian cancer
    a. 18 years of age or older
    b. Used as a single agent for persistent or recurrent disease

Prior – Approval *Renewal* Requirements

No renewal for resectable melanoma diagnosis

Diagnoses

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

1. Unresectable or metastatic melanoma
    a. 18 years of age or older
    b. Used as a single agent **OR** used in combination with dabrafenib (Tafinlar)

2. Metastatic non-small cell lung cancer (NSCLC)
    a. 18 years of age or older
    b. Used in combination with dabrafenib (Tafinlar)

3. Locally advanced or metastatic anaplastic thyroid cancer (ATC)
    a. 18 years of age or older
    b. Used in combination with dabrafenib (Tafinlar)

4. Unresectable or metastatic solid tumors
    a. 1 year of age or older
    b. Used in combination with dabrafenib (Tafinlar)

5. Low-grade glioma (LGG)
    a. 1 year of age or older

b. Used in combination with dabrafenib (Tafinlar)

6. Low-grade serous ovarian cancer
   a. 18 years of age or older
   b. Used as a single agent for persistent or recurrent disease

AND the following for **ALL** indications:

a. **NO** disease progression or unacceptable toxicity

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity

Strength	Quantity
0.5 mg	2 mg per day
2 mg	
0.05 mg/mL oral solution	

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

No renewal for resectable melanoma diagnosis

Rationale

Summary

Mekinist (trametinib) is indicated for the treatment of unresectable or metastatic melanoma, resectable melanoma, metastatic non-small cell lung cancer (NSCLC), locally advanced or metastatic anaplastic thyroid cancer (ATC), unresectable or metastatic solid tumors, and low-grade glioma (LGG). Mekinist is also used off-label for the treatment of low-grade serous ovarian cancer. 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 embryo-fetal toxicity and impaired fertility (1-3).

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

References

1. Mekinist [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; August 2023.
2. NCCN Clinical Practice Guidelines in Oncology® Ovarian Cancer (Version 2.2023). National Comprehensive Cancer Network, Inc. June 2023. Accessed on November 2, 2023.
3. NCCN Drugs & Biologics Compendium® Trametinib 2023. National Comprehensive Cancer Network, Inc. Accessed on November 2, 2023.

Policy History

Date	Action
June 2013	New Policy
September 2013	Annual editorial and reference update. Addition to criteria to allow combination therapy with Tafinlar.
February 2014	Aligned criteria to new package insert. Revised the requirement that the patient must have NO prior BRAF therapy pertains to Mekinist used as a single agent only. Addition of new warnings and precautions with the combined therapy: new malignancies, hemorrhages, and venous thromboembolism.
September 2014	Annual editorial and reference update
December 2014	Annual editorial and reference update Removal of warnings and precautions: Assess left ventricular ejection fraction (LVEF), absence of symptomatic congestive heart failure, interstitial lung disease (ILD), retinal vein occlusion
June 2015	Annual review
March 2016	Annual editorial review and reference update Policy number change from 5.04.38 to 5.21.38
June 2016	Annual editorial review and reference update Addition of non-small cell lung cancer (NSCLC)

	Removal of the requirement: if Mekinist is used as a single agent only that the patient must have NO prior BRAF inhibitor treatment
June 2017	Annual editorial review and reference update
June 2018	Annual review and reference update Addition of the diagnoses of resectable melanoma and locally advanced or metastatic anaplastic thyroid cancer to criteria Addition of quantity limits to criteria and combination with Tafinlar requirements in renewal section
September 2018	Annual editorial review
June 2019	Annual review and reference update
June 2020	Annual review and reference update
June 2021	Annual review and reference update
November 2021	Addition of indication: low-grade serous ovarian cancer, per reconsideration review
March 2022	Annual review and reference update
July 2022	Addition of indication: BRAF V600E mutation-positive unresectable or metastatic solid tumors. Simplified or changed renewal requirements for consistency
September 2022	Annual review and reference update
April 2023	Per PI update, added indication of low-grade glioma (LGG). Added 0.05 mg/mL oral solution and changed PA limit to 2 mg per day of all strengths and dosage forms. Removed initiation requirement for an FDA-approved test for ATC indication
June 2023	Annual review and reference update
October 2023	Per PI update, lowered age requirement for unresectable or metastatic solid tumors from 6 years and older to 1 year and older
December 2023	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 8, 2023 and is effective on January 1, 2024.