BlueCross BlueShield Federal Employee Program

MEKINIST (trametinib)

RATIONALE FOR INCLUSION IN PA PROGRAM

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.

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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).

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; March 2024.
2. NCCN Clinical Practice Guidelines in Oncology® Ovarian Cancer (Version 1.2024). National Comprehensive Cancer Network, Inc. January 2024. Accessed on April 15, 2024.

3. NCCN Drugs & Biologics Compendium® Trametinib 2024. National Comprehensive Cancer Network, Inc. Accessed on April 15, 2024.