Tafinlar

Description

Tafinlar (dabrafenib)

Background
Tafinlar, a BRAF inhibitor, is used as a single agent for the treatment of advanced (metastatic) or unresectable (cannot be removed by surgery) melanomas that express the BRAF V600E gene mutation or in combination with Mekinist (trametinib) for the BRAF V600E or V600K mutations. Tafinlar can also be used for resectable melanoma (can also be considered stage III or locally advanced) in combination with trametinib, for the adjuvant treatment of patients with melanoma with BRAF V600E or V600K mutations. Additionally, Tafinlar in combination with trametinib 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. 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. Tafinlar is not indicated for the treatment of wild-type BRAF gene mutation (1-4).

Mekinist and Tafinlar, combined use, 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: Tafinlar is a kinase inhibitor indicated as: (1)
1. Single agent for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation when used as a single agent and indicated for BRAF V600E.

2. Combination treatment with trametinib (Mekinist) 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 trametinib (Mekinist) 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 trametinib (Mekinist) 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:
Tafinlar is not indicated for treatment of patients with wild-type BRAF melanoma (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)

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

Cardiomyopathy can occur when Tafinlar is used in combination with trametinib and with trametinib as a single agent. Assess left ventricular ejection fraction (LVEF) by echocardiogram or multigated acquisition (MUGA) scan before initiation of Tafinlar in combination with trametinib, one month after initiation, and then at 2- to 3-month intervals while on treatment with the combination. Withhold treatment with trametinib and continue Tafinlar at the same dose if absolute LVEF value decreases by 10% from pretreatment values and is less than the lower limit of normal. For symptomatic cardiomyopathy or persistent, asymptomatic LV dysfunction...
that does not resolve within 4 weeks, permanently discontinue trametinib and withhold Tafinlar. Resume Tafinlar at the same dose level upon recovery of cardiac function (1).

Retinal pigment epithelial detachments (RPED) can occur when Tafinlar is used in combination with trametinib. Retinal detachments resulting from trametinib are often bilateral and multifocal, occurring in the macular region of the retina (1).

Tafinlar results in an increased incidence of cutaneous squamous cell carcinoma, keratoacanthoma, and melanoma. Dermatologic evaluations must be performed prior to initiation of therapy, every 2 months while on therapy, and for up to 6 months following discontinuation of Tafinlar (1).

Serious febrile drug reactions, defined as serious cases of fever or fever of any severity accompanied by hypotension, rigors or chills, dehydration, or renal failure in the absence of another identifiable cause (such as infection) have occurred. Withhold Tafinlar for fever 101.3°F or greater or any complicated fever and evaluate for signs and symptoms of infection. Prophylaxis with antipyretics may be required when resuming Tafinlar (1).

Tafinlar treatment may increase blood sugar levels requiring changes in diabetes medication or the need to start medicines to control diabetes. Serum glucose levels should be monitored as clinically appropriate during treatment with Tafinlar in patients with pre-existing diabetes or hyperglycemia (1).

There is a potential risk of hemolytic anemia in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency, uveitis (including iritis), and embryo fetal toxicity. Patients with G6PD deficiency must be monitored for signs of hemolytic anemia. Patients must be monitored for visual signs and symptoms of uveitis. Female patients of reproductive potential should be advised to use a highly effective non-hormonal method of contraception during treatment and for 4 weeks after treatment since Tafinlar can render hormonal contraceptives ineffective. Male patients must be advised of potential risk for impaired spermatogenesis (1).

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

**Related Policies**
Braftovi, Cotellic, Mekinist, Mektovi, Zelboraf
This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Tafinlar 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.

Tafinlar 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
   a. Physician agrees to perform dermatologic evaluation prior to initiation, every 2 months while on therapy, and for up to 6 months following discontinuation of therapy
   b. Patient must NOT have wild-type BRAF melanoma

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

2. Resectable melanoma
   a. Used in combination with trametinib (Mekinist) 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)
4. Locally advanced or metastatic anaplastic thyroid cancer (ATC)
   a. Used in combination with trametinib (Mekinist) with documented BRAF V600E mutation as detected by an FDA-approved test
   b. **NO** satisfactory locoregional treatment options

**Prior – Approval Renewal Requirements**

**Age**
18 years of age and older

**Diagnoses**

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

1. Unresectable or metastatic melanoma
   a. Physician agrees to perform dermatologic evaluations every two months while on therapy and up to 6 months following discontinuation of therapy

   **AND ONE** of the following:
   1. Used as a single agent with documented BRAF V600E mutation as detected by an FDA-approved test
   2. Used in combination with trametinib (Mekinist) 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 trametinib (Mekinist) 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 trametinib (Mekinist) with documented BRAF V600E mutation as detected by an FDA-approved test

   **AND ALL** of the following for **ALL** diagnoses:
   a. Absence of disease progression

**Policy Guidelines**
Pre - PA Allowance
None

Prior - Approval Limits

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Duration 12 months

Prior – Approval *Renewal* Limits
Same as above

No renewal for resectable melanoma diagnosis

Rationale

Summary
Tafinlar is approved for patients 18 years of age or older for unresectable or metastatic melanoma with BRAF V600E mutation in which the BRAF V600E mutation. Tafinlar can also be used for resectable melanoma (can also be considered stage III or locally advanced) in combination with trametinib, for the adjuvant treatment of patients with melanoma with BRAF V600E or V600K mutations following complete resection. Additionally, Tafinlar in combination with trametinib 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. Tafinlar is not indicated for patients with wild-type BRAF. Tafinlar results in an increased incidence of cutaneous squamous cell carcinoma, keratoacanthoma, and melanoma. Tafinlar may cause drug-induced fevers. Withhold Tafinlar for fever 101.3°F or greater or any complicated fever and evaluate for signs and symptoms of infection. Tafinlar treatment may increase blood sugar levels. There is a potential risk of hemolytic anemia in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency, uveitis (including iritis), and embryofetal toxicity. The safety and effectiveness of Tafinlar have not been established in pediatric patients (1-3).

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

References

Policy History

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<tr>
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<tbody>
<tr>
<td>June 2013</td>
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| September 2013 | Annual editorial and reference update.  
|             | Addition to criteria to allow combination therapy with Mekinist.                                     |
| February 2014 | Aligned criteria to new package insert.  
|             | Addition of new warnings and precautions with the combined therapy with Mekinist.                    |
| June 2014  | Annual editorial and reference update.                                                               |
| December 2014 | Annual editorial and reference update.  
|             | Removal of warnings and precautions with the combined therapy with Mekinist.                         |
| June 2015  | Annual review                                                                                       |
| March 2016 | Annual editorial review and reference update  
|             | Policy number change from 5.04.37 to 5.21.37                                                         |
| June 2016  | Annual editorial review and reference update  
|             | Addition of Non-Small Cell Lung Cancer (NSCLC)                                                        |
| June 2017  | Annual editorial review and reference update  
|             | Rearranged the requirement of physician agrees to perform dermatologic evaluation prior to initiation, every 2 months while on therapy, and for up to 6 months following discontinuation of therapy and patient must NOT have wild-type BRAF melanoma -- put it under the melanoma indication only. |
| 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 and combination with Mekinist requirements in renewal section              |
| September 2018 | Annual editorial review and reference update                                                          |
| June 2019  | Annual review and reference update                                                                   |

Keywords

- Tafinlar
- Prescription Drugs
- Antineoplastic Agents
- Melanoma
- Mekinist
- Non-Small Cell Lung Cancer
- Wild-type BRAF melanoma
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This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 20, 2019 and is effective on July 1, 2019.