Tafinlar® (dabrafenib)

Mekinist® (trametinib)

BRAF+

Abbreviated Prescribing Information TAFINLAR® (dabrafenib) 50 mg and 75 mg Hard capsules

Important note: Before prescribing, consult full prescribing information of TAFINLAR® (dabrafenib). When used in combination with MEKINIST® (trametinib), consult full prescribing information of both products. **Presentation:** Hard capsules: contain dabrafenib mesylate equivalent to 50 mg or 75 mg of dabrafenib. **Indications:** As monotherapy or in combination with Mekinist® for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600 mutation. In combination with Mekinist: for the adjuvant treatment of patients with Stage III melanoma with a BRAF V600 mutation following complete resection, for the treatment of patients with advanced non-small cell lung cancer (NSCLC) with a BRAF V600 mutation, and for the treatment of patients with locally advanced or metastatic anaplastic thyroid cancer (ATC) with a BRAF V600 mutation. **Dosage and administration: Adults:** Recommended dose either as monotherapy or in combination with Mekinist is 150 mg twice daily. Tafinlar should be taken without food, with water, either at least one hour before, or at least two hours after a meal with an interval of approximately 12 hours between doses. Tafinlar should be taken at similar times every day. When Tafinlar is taken in combination with Mekinist, the once-daily dose of Mekinist should be taken at the same time each day with the daily dose of Tafinlar. **Missed dose:** The missed dose should be taken only if it is more than 6 hours until the next scheduled dose. **Dose modifications:** Management of adverse reactions may require treatment interruption, dose reduction or treatment discontinuation. **Special populations: Children (<18 years):** Safety and efficacy not established. **Elderly (>65 years):** No dose adjustment required. **Renal impairment:** Mild or moderate: No dose adjustment required. Severe: Should be used with caution. **Hepatic impairment:** Mild: No dose adjustment required. Moderate or severe: Should be used with caution. **Contraindications:** None. **Warnings and precautions: Pyrexia:** Pyrexia including severe rigors, dehydration and hypotension (including acute renal insufficiency) reported. Incidence and severity increased when used in combination with Mekinist. Monitoring serum creatinine and renal function. Serious non-infectious febrile events observed. For management of pyrexia, therapy should be interrupted if the patient's temperature is ≥38°C (100.4°F). In case of recurrence, therapy can also be interrupted at the first symptom of pyrexia. **Cutaneous malignancies (Cutaneous squamous cell carcinoma and New primary melanoma):** Skin examination prior, during, and for 6 months after discontinuation of treatment or until initiation of another anti-neoplastic therapy. **Non-cutaneous malignancies:** Monitoring as clinically appropriate. In case of a RAS positive mutation benefits and risks to be considered before continuing treatment. No Mekinist dose modification required when taken in combination with Tafinlar. **Pancreatitis:** Unexplained abdominal pain should be promptly investigated to include measurement of serum amylase and lipase. Close monitoring when re-starting Tafinlar. **Uveitis:** Monitoring patients for visual signs and symptoms during therapy. **Hemorrhage:** Hemorrhagic events (includes major and fatal) occurred in patients taking Tafinlar in combination with Mekinist. **Venous thrombo-embolism (VTE):** VTE, including deep vein thrombosis (DVT) and pulmonary embolism (PE) can occur when Tafinlar is used in combination with Mekinist. Patients should be advised to immediately seek medical care if they develop symptoms of VTE. **Severe cutaneous adverse reactions (SCARs):** SCARs, including Stevens-Johnson syndrome, and drug reaction with eosinophilia and systemic symptoms (DRESS), which can be life-threatening or fatal, have been reported with Tafinlar in combination with Mekinist. Before initiating treatment, patients should be advised of the signs and symptoms and monitored closely for skin reactions. If signs and symptoms suggestive of SCARs appear, Tafinlar and Mekinist should be withdrawn. **Pregnancy, lactation, females and males of reproductive potential: Pregnancy:** Tafinlar can be harmful to the fetus. Pregnant women should be advised of the potential risk to the fetus. **Lactation:** Nursing women should be advised of the potential risks to the child. **Females and males of reproductive potential:** Sexually-active women should be advised to use effective contraception while on Tafinlar and for at least 2 weeks after stopping it. If taken in combination with Mekinist, effective contraception should be used while on treatment and for at least 16 weeks after stopping it. Efficacy of oral or any other systemic hormonal contraceptives may be decreased; an effective alternative method of contraception should be used. Males (including those that have had a vasectomy) should be advised to use condoms while on Tafinlar and for at least 2 weeks after stopping it. If taken in combination with Mekinist, condoms should be used while on treatment and for at least 16 weeks after stopping it. **Infertility:** Potential risk for impaired spermatogenesis, which may be irreversible. **Adverse events with Tafinlar monotherapy in metastatic melanoma: Very common (≥10%):** papilloma, decreased appetite, headache, cough, nausea, vomiting, diarrhoea, skin effects (rash, hyperkeratosis), alopecia, palmar-plantar erythrodysesthesia syndrome, arthralgia, myalgia, pain in extremity, asthenia, chills, fatigue, pyrexia. **Common (1 to 10%):** nasopharyngitis, acrochordon (skin tags), cutaneous squamous cell carcinoma (SCC) including SCC of the skin, SCC in situ (Bowen's disease) and keratoacanthoma, seborrheic keratosis, hypophosphataemia, hyperglycaemia, constipation, skin effects (actinic keratosis, skin lesion, dry skin, erythema, pruritus), photosensitivity, influenza-like illness. **Uncommon (0.1 to 1%):** new primary melanoma, hypersensitivity, uveitis, pancreatitis, panniculitis, renal failure, acute renal failure, tubulointerstitial nephritis. **Adverse events in combination with Mekinist in metastatic melanoma: Very common (≥10%):** urinary tract infection, nasopharyngitis, neutropenia, decreased appetite, headache, dizziness, hypertension, haemorrhage, cough, abdominal pain, constipation, diarrhoea, nausea, vomiting, dry skin, pruritus, rash, dermatitis acneiform, arthralgia, myalgia, pain in extremity, fatigue, oedema peripheral, pyrexia, chills, asthenia, alanine aminotransferase increased, aspartate aminotransferase increased. **Common (1 to 10%):** cellulitis, folliculitis, paronychia, rash pustular, cutaneous squamous cell carcinoma (SCC) including SCC of the skin, SCC in situ (Bowen's disease) and keratoacanthoma, papilloma including skin papilloma, seborrheic keratosis, acrochordon (skin tags), anaemia, thrombocytopenia, leukopenia, dehydration, hyperglycaemia, hyponatraemia, hypophosphataemia, vision blurred, visual impairment, ejection fraction decreased, bradycardia, hypotension, lymphoedema, dyspnoea, dry mouth, stomatitis, erythema, actinic keratosis, night sweats, hyperkeratosis, alopecia, palmar-plantar erythrodysesthesia syndrome, skin lesion, hyperhidrosis, skin fissures, panniculitis, photosensitivity, muscle spasms, blood creatine phosphokinase increased, renal failure, mucosal inflammation, influenza-like illness, face oedema, blood alkaline phosphatase increased, gamma-glutamyltransferase increased. **Uncommon (0.1 to 1%):** new primary melanoma, hypersensitivity, chorioretinopathy, uveitis, retinal detachment, periorbital oedema, left ventricular dysfunction, cardiac failure, pneumonitis, interstitial lung disease, gastrointestinal perforation, colitis, pancreatitis, rhabdomyolysis, nephritis, renal failure acute. Adverse drug reactions in combination with Mekinist in Stage III melanoma following complete resection. **Very common (≥10%):** nasopharyngitis, neutropenia, decreased appetite, headache, dizziness, haemorrhage, hypertension, cough, nausea, diarrhoea, vomiting, abdominal pain, constipation, rash, dry skin, dermatitis acneiform, erythema, pruritus, arthralgia, myalgia, pain in extremity, muscle spasms, pyrexia, fatigue, chills, oedema peripheral, influenza-like illness, alanine aminotransferase increased, aspartate aminotransferase increased. **Common (1 to 10%):** uveitis, chorioretinopathy, retinal detachment, palmar-plantar erythrodysesthesia syndrome, alkaline phosphatase increased, ejection fraction decreased. **Uncommon (0.1 to 1%):** rhabdomyolysis, renal failure. **Adverse drug reactions in combination with Mekinist in advanced non-small cell lung cancer; Very common (≥10%):** neutropenia, hyponatraemia, headache, dizziness, haemorrhage, hypotension, nausea, vomiting, diarrhoea, decreased appetite, constipation, erythema, dry skin, rash, pruritus, hyperkeratosis incl. hyperkeratosis, actinic and seborrheic keratosis and keratosis pilaris, muscle spasms, arthralgia, myalgia, pyrexia, asthenia including fatigue and malaise, oedema (generalized and peripheral), chills, blood alkaline phosphatase increased, aspartate aminotransferase increased, alanine aminotransferase increased. **Common (1 to 10%):** cutaneous squamous cell carcinoma, leukopenia, dehydration, detachment of retina/retinal pigment epithelium, ejection fraction decreased, hypertension, pulmonary embolism, pancreatitis acute, renal failure, tubulointerstitial nephritis. *For a complete list, consult full prescribing information.* **Adverse drug reactions in combination with Mekinist in locally advanced or metastatic anaplastic thyroid cancer (ATC): Very common (≥10%):** neutropenia, anaemia, leukopenia, hyperglycaemia, decreased appetite, headache, dizziness, haemorrhage, cough, nausea, vomiting, diarrhoea, constipation, dry mouth, rash, myalgia, arthralgia, fatigue, pyrexia, chills, oedema, alanine aminotransferase increased, aspartate aminotransferase increased, blood alkaline phosphatase increased. **Common (1 to 10%):** hypophosphataemia, hyponatraemia, detachment of retinal pigment epithelium, hypertension, rhabdomyolysis, ejection fraction decreased. **Adverse drug reactions in combination with Mekinist from post-marketing experience and pooled clinical trials: Common (1 to 10%):** VTE. **Uncommon (0.1 to 1%):** Sarcoidosis. *For a complete list, consult full prescribing information.* **Interactions:** Strong inhibitors or inducers of CYP2C8 or CYP3A4 likely increase or decrease, respectively, Tafinlar concentration. Alternative agents should be considered during administration with Tafinlar. Tafinlar induces CYP3A4, CYP2C9, and may induce CYP2B6, CYP2C8, CYP2C19, UGT and P-gp. Efficacy of medicinal products metabolized by these enzymes may be reduced. Monitoring recommended. Alternative agents should be considered during administration with Tafinlar. Tafinlar inhibits OATP1B1 and OATP1B3. Monitoring recommended of drugs that are sensitive substrates of OATP1B1 and OATP1B3 and are known to have a narrow therapeutic index with regards to high peak concentrations (Cmax). **Packs and prices:** Country-specific. **Legal classification:** Country-specific.

Abbreviated Prescribing Information MEKINIST® (trametinib) 0.5 mg and 2 mg Film-coated tablets

Important note: Before prescribing, consult full prescribing information of MEKINIST® (trametinib). When used in combination with TAFINLAR® (dabrafenib), consult full prescribing information of both products. **Presentation:** Film-coated tablets: contain trametinib dimethyl sulfoxide equivalent to 0.5 mg and 2 mg of trametinib. **Indications:** As monotherapy or in combination with Tafinlar® for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600 mutation. As monotherapy, has not demonstrated clinical activity in patients who progressed on a prior BRAF inhibitor therapy. In combination with Tafinlar: for the adjuvant treatment of patients with Stage III melanoma with a BRAF V600 mutation following complete resection, for the treatment of patients with advanced non-small cell lung cancer (NSCLC) with a BRAF V600 mutation, and for the treatment of patients with locally advanced or metastatic anaplastic thyroid cancer (ATC) with a BRAF V600 mutation. **Dosage and administration: Adults:** Recommended dose either as monotherapy or in combination with Tafinlar is 2 mg once daily. Mekinist should be taken without food, with a full glass of water, at least 1 hour before or at least 2 hours after a meal. When Mekinist is taken in combination with Tafinlar, the once-daily dose of Mekinist should be taken at the same time each day with either the morning or the evening dose of Tafinlar. ***Missed dose:*** A missed dose should be taken only if it is more than 12 hours until the next scheduled dose. ***Dose modifications:*** Management of adverse reactions may require treatment interruption, dose reduction or treatment discontinuation. **Special populations: Children (<18 years):** Safety and efficacy not established. **Elderly (> 65 years):** No dose adjustment required. **Renal impairment:** ***Mild or moderate:*** No dose adjustment required. ***Severe:*** Should be used with caution. **Hepatic impairment:** ***Mild:*** No dose adjustment required. ***Moderate or severe:*** Should be used with caution. **Contraindications:** None. **Warnings and precautions: Left ventricular ejection fraction (LVEF) reduction/Left ventricular dysfunction:** Cases of LVEF decrease reported. Should be used with caution when conditions could impair left ventricular function. All patients should be evaluated for LVEF prior to initiation of treatment with continued evaluation during treatment. Dose modification guidelines should be considered. **Hemorrhage:** Hemorrhagic events, including major and fatal hemorrhagic events occurred in patients taking Mekinist as monotherapy and in combination with Tafinlar. **Visual impairment:** Visual disturbances, including chorioretinopathy or retinal pigment epithelial detachment (RPED) and retinal vein occlusion (RVO) observed. Not recommended for patients with history of RVO. Ophthalmological evaluation should be performed at baseline and during treatment. If retinal abnormalities observed, treatment should be interrupted immediately and referral to specialist should be considered. Permanent discontinuation of treatment if RVO occurs. **Rash:** Observed in Mekinist monotherapy and in combination with Tafinlar. **Severe cutaneous adverse reactions (SCARs):** SCARs, including Stevens-Johnson syndrome, and drug reaction with eosinophilia and systemic symptoms (DRESS), which can be life-threatening or fatal, have been reported with Mekinist in combination with Tafinlar. Before initiating treatment, patients should be advised of the signs and symptoms and monitored closely for skin reactions. If signs and symptoms suggestive of SCARs appear, Mekinist and Tafinlar should be withdrawn. Venous thrombo-embolism (VTE): VTE including deep vein thrombosis (DVT) and pulmonary embolism (PE) can occur when used as monotherapy or in combination with Tafinlar. Patients should seek immediate medical care if they develop symptoms of VTE. **Pyrexia:** Pyrexia including severe rigors, dehydration and hypotension (including acute renal insufficiency) reported. Incidence and severity increased when Mekinist used in combination with Tafinlar. Monitoring serum creatinine and other evidence of renal function impairment during and following severe pyrexia events. Serious non-infectious febrile events observed. For management of pyrexia, therapy should be interrupted if the patient's temperature is ≥38°C (100.4°F). In case of recurrence, therapy can also be interrupted at the first symptom of pyrexia. **Colitis and Gastrointestinal perforation:** Colitis and gastrointestinal perforation, including fatal outcome, reported. Treatment with Mekinist as monotherapy or in combination with Tafinlar should be used with caution in patients with risk factors for gastrointestinal perforation, including a history of diverticulitis, metastases to the gastrointestinal tract and concomitant use of medications with a recognized risk of gastrointestinal perforation. If patients develop symptoms of colitis and gastrointestinal perforation they should immediately seek medical care. **Pregnancy, lactation, females and males of reproductive potential: Pregnancy:** Mekinist can be harmful to the fetus. Pregnant women should be advised of the potential risk to the fetus. **Lactation:** Nursing women should be advised of the potential risks to the child. **Females and males of reproductive potential:** Sexually-active women should be advised to use effective contraception while on Mekinist and for at least 16 weeks after stopping it. Efficacy of oral or any other systemic hormonal contraceptives may be decreased; an effective alternative method of contraception should be used. Male patients (including those that have had a vasectomy) should be advised to use condoms while on Mekinist and for at least 16 weeks after stopping it. **Infertility:** May impair human fertility. **Adverse events with Mekinist monotherapy in metastatic melanoma: Very common (≥10%):** hypertension, haemorrhage, cough, dyspnoea, diarrhoea, nausea, vomiting, constipation, abdominal pain, dry mouth, rash, dermatitis acneiform, dry skin, pruritus, alopecia, fatigue, oedema peripheral, pyrexia. **Common (1 to 10%):** hypersensitivity, folliculitis, paronychia, cellulitis, rash pustular, anaemia, dehydration, vision blurred, periorbital oedema, visual impairment, left ventricular dysfunction, ejection fraction decreased, bradycardia, lymphoedema, epistaxis, pneumonitis, stomatitis, skin chapped, erythema, palmar-plantar erythrodysaesthesia syndrome, skin fissures, blood creatine phosphokinase increased, face oedema, mucosal inflammation, asthenia, aspartate aminotransferase increased, alanine aminotransferase increased, blood alkaline phosphatase increased. **Uncommon (0.1 to 1%):** chorioretinopathy, retinal vein occlusion, papilloedema, retinal detachment, cardiac failure, interstitial lung disease, gastrointestinal perforation, colitis, rhabdomyolysis. **Adverse events in combination with Tafinlar in metastatic melanoma: Very common (≥10%):** urinary tract infection, nasopharyngitis, neutropenia, decreased appetite, headache, dizziness, hypertension, haemorrhage, cough, abdominal pain, constipation, diarrhoea, nausea, vomiting, dry skin, pruritus, rash, dermatitis acneiform, arthralgia, myalgia, pain in extremity, fatigue, oedema peripheral, pyrexia, chills, asthenia, alanine aminotransferase increased, aspartate aminotransferase increased. **Common (1 to 10%):** cellulitis, folliculitis, paronychia, rash pustular, cutaneous squamous cell carcinoma (SCC) including SCC of the skin, SCC in situ (Bowen's disease) and keratoacanthoma, papilloma including skin papilloma, seborrheic keratosis, acrochordon (skin tags), anaemia, thrombocytopenia, leukopenia, dehydration, hyperglycaemia, hyponatraemia, hypophosphataemia, vision blurred, visual impairment, ejection fraction decreased, bradycardia, hypotension, lymphoedema, dyspnoea, dry mouth, stomatitis, erythema, actinic keratosis, night sweats, hyperkeratosis, alopecia, palmar-plantar erythrodysesthesia syndrome, skin lesion, hyperhidrosis, skin fissures, panniculitis, photosensitivity, muscle spasms, blood creatine phosphokinase increased, renal failure, mucosal inflammation, influenza-like illness, face oedema, blood alkaline phosphatase increased, gamma-glutamyltransferase increased. **Uncommon (0.1 to 1%):** new primary melanoma, hypersensitivity, chorioretinopathy, uveitis, retinal detachment, periorbital oedema, left ventricular dysfunction, cardiac failure, pneumonitis, interstitial lung disease, pancreatitis, gastrointestinal perforation, colitis, rhabdomyolysis, nephritis, renal failure acute. **Adverse drug reactions in combination with Tafinlar in Stage III melanoma following complete resection: Very common (≥10%):** nasopharyngitis, neutropenia, decreased appetite, headache, dizziness, haemorrhage, hypertension, cough, nausea, diarrhoea, vomiting, abdominal pain, constipation, rash, dry skin, dermatitis acneiform, erythema, pruritus, arthralgia, myalgia, pain in extremity, muscle spasms, pyrexia, fatigue, chills, oedema peripheral, influenza like illness, alanine aminotransferase increased, aspartate aminotransferase increased. **Common (1 to 10%):** uveitis, chorioretinopathy, retinal detachment, palmar-plantar erythrodysesthesia syndrome, alkaline phosphatase increased, ejection fraction decreased. **Uncommon (0.1 to 1%):** rhabdomyolysis, renal failure. **Adverse drug reactions in combination with Tafinlar in advanced non-small cell lung cancer: Very common (≥10%):** neutropenia, hyponatraemia, headache, dizziness, haemorrhage, hypotension, nausea, vomiting, diarrhoea, decreased appetite, constipation, erythema, dry skin, rash, pruritus, hyperkeratosis incl. hyperkeratosis, actinic and seborrheic keratosis and keratosis pilaris, muscle spasms, arthralgia, myalgia, pyrexia, asthenia incl. fatigue and malaise, oedema (generalized and peripheral), chills, blood alkaline phosphatase increased, aspartate aminotransferase increased, alanine aminotransferase increased. **Common (1 to 10%):** cutaneous squamous cell carcinoma, leukopenia, dehydration, detachment of retina/retinal pigment epithelium, ejection fraction decreased, hypertension, pulmonary embolism, pancreatitis acute, renal failure, tubulointerstitial nephritis. **Adverse drug reactions in combination with Tafinlar in locally advanced or metastatic anaplastic thyroid cancer (ATC): Very common (≥10%):** neutropenia, anaemia, leukopenia, hyperglycaemia, decreased appetite, headache, dizziness, haemorrhage, cough, nausea, vomiting, diarrhoea, constipation, dry mouth, rash, myalgia, arthralgia, fatigue, pyrexia, chills, oedema, alanine aminotransferase increased, aspartate aminotransferase increased, blood alkaline phosphatase increased. **Common (1 to 10%):** hypophosphataemia, hyponatraemia, detachment of retinal pigment epithelium, hypertension, rhabdomyolysis, ejection fraction decreased. **Adverse drug reactions in combination with Tafinlar from post-marketing experience and pooled clinical trials: Common (1 to 10%):** VTE. **Uncommon (0.1 to 1%):** Sarcoidosis For a complete list, consult full prescribing information. **Interactions:** None. **Packs and prices:** Country-specific. **Legal classification:** Country-specific. agents should be considered during administration with Tafinlar. Tafinlar inhibits OATP1B1 and OATP1B3. Monitoring recommended of drugs that are sensitive substrates of OATP1B1 and OATP1B3 and are known to have a narrow therapeutic index with regards to high peak concentrations (Cmax). **Packs and prices:** Country-specific. **Legal classification:** Country-specific.

โปรดอ่านรายละเอียดเพิ่มเติมในเอกสารกำกับยา
ใบอนุญาตโฆษณาเลขที่ ขศ 1281/2560

ต้องติดตาม
เป็นยาใหม่ใช้เฉพาะโรงพยาบาล
แพทย์ควรติดตามผลการใช้ยา

NOVARTIS

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