

RAFINLAR®

Important note: Before prescribing, consult full prescribing information of RAFINLAR® (dabrafenib). When used in combination with MEQSEL® (trametinib), consult full prescribing information of both products.

Presentation: Hard capsules: contain dabrafenib mesylate equivalent to 50 mg or 75 mg of dabrafenib.

Indications:

BRAF V600E Mutation-Positive Unresectable or Metastatic Melanoma

Dabrafenib is indicated as a single agent for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation as detected by an appropriate test.

BRAF V600E Mutation-Positive Unresectable or Metastatic Melanoma

Dabrafenib is indicated, in combination with trametinib, for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutations, as detected by an appropriate test.

BRAF V600E Mutation-Positive Metastatic NSCLC

Dabrafenib is indicated, in combination with trametinib, for the treatment of adult patients with advanced non-small cell lung cancer (NSCLC) with a BRAF V600 mutation.

Adjuvant Treatment of BRAF V600E or V600K Mutation-Positive Melanoma

Dabrafenib in combination with trametinib for the adjuvant treatment of patients with melanoma with BRAF V600E or V600K mutations, as detected by an appropriate test, and involvement of lymph node(s), following complete resection.

BRAF V600E Mutation-Positive Locally Advanced or Metastatic Anaplastic Thyroid Cancer

Dabrafenib is indicated, in combination with trametinib, for the treatment of patients with locally advanced or metastatic anaplastic thyroid cancer (ATC) with BRAF V600E mutation and with no satisfactory locoregional treatment options.

BRAF V600E Mutation-Positive Unresectable or Metastatic Solid Tumors

Dabrafenib is indicated, in combination with trametinib, for the treatment of adult and pediatric patients 6 years 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.

Limitations of Use:

Dabrafenib is not indicated for treatment of patients with colorectal cancer because of known intrinsic resistance to BRAF inhibition.

Dabrafenib is not indicated for treatment of patients with wild-type BRAF solid tumors.

Dosage and administration: ♦**Adults:** Recommended dose either as monotherapy or in combination with trametinib is 150 mg twice daily (corresponding to a total daily dose of 300 mg). *Pediatrics:* The recommended dosage for Dabrafenib in pediatric patients who weigh at least 26 kg, is based on body weight. A recommended dose of Dabrafenib for patients who weigh less than 26 kg has not been established. ♦ Dabrafenib should not be used in patients with wild-type BRAF solid tumors. Dabrafenib in combination with trametinib should not be used in patients with colorectal cancer due to intrinsic resistance to BRAF inhibition. ♦ Dabrafenib should be taken without food either at least one hour before, or at least two hours after a meal with an interval of approximately 12 hours between doses. Dabrafenib should be taken at similar times every day. ♦When dabrafenib is taken in combination with trametinib, the once-daily dose of trametinib should be taken at the same time each day with the daily dose of dabrafenib. ♦**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 (<6 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 trametinib. 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 $\geq 38^{\circ}\text{C}$ (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 trametinib dose modification required when taken in combination with dabrafenib. ♦**Pancreatitis:** Unexplained abdominal pain should be promptly investigated to include measurement of serum amylase and lipase. Close monitoring when re-starting dabrafenib. ♦**Uveitis:** Monitoring patients for visual signs and symptoms during therapy. ♦**Hemorrhage:** Hemorrhagic events (includes major and fatal) occurred in patients taking dabrafenib in combination with trametinib. ♦**Venous thrombo-embolism (VTE):** VTE, including deep vein thrombosis (DVT) and pulmonary embolism (PE) can occur when dabrafenib is used in combination with trametinib. 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 dabrafenib in combination with trametinib. 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, dabrafenib and trametinib should be withdrawn. ♦**Hemophagocytic lymphohistiocytosis (HLH):** In post-marketing experience, HLH has been observed with dabrafenib in combination with trametinib. If HLH is suspected, treatment should be interrupted. If HLH is confirmed, treatment should be discontinued and appropriate management of HLH should be initiated.

Pregnancy, lactation, females and males of reproductive potential:

Pregnancy: Dabrafenib 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 dabrafenib and for at least 2 weeks after stopping it. If taken in combination with trametinib, 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 dabrafenib and for at least 2 weeks after stopping it. If taken in combination with trametinib, 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 Dabrafenib 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 Trametinib 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 Trametinib 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 Trametinib 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 Trametinib in locally advanced or metastatic anaplastic thyroid cancer (ATC):

Very common (≥10%): neutropenia, anaemia, leukopenia, hyperglycemia, 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 with Dabrafenib monotherapy from post-marketing experience and pooled clinical trials

Common (≥1 to <10%): peripheral neuropathy.

Adverse drug reactions with Dabrafenib in combination with Trametinib from post-marketing

experience and pooled clinical trials:

Common (≥ 1 to $< 10\%$): VTE, peripheral neuropathy, atrioventricular block.

Uncommon (≥ 0.1 to $< 1\%$): sarcoidosis, bundle branch block.

Not known: haemophagocytic lymphohistiocytosis.

For a complete list, consult full prescribing information.

Interactions: ♦ Strong inhibitors or inducers of CYP2C8 or CYP3A4 likely increase or decrease, respectively, dabrafenib concentration. Alternative agents should be considered during administration with dabrafenib. ♦ Dabrafenib 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 dabrafenib. ♦ Dabrafenib 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 (C_{max}).

Packs: 28 capsules

Before prescribing, please consult full prescribing information available from Novartis Healthcare Private Limited, Inspire BKC, 7th floor, Bandra Kurla Complex, Bandra (East), Mumbai – 400 051, Maharashtra, India. Tel + 91 22 50243000

For the use of only oncologist.

India BSS dated 30 Aug 2024 based on international BSS dated 05 Feb 2024 effective from 20 May 2025.