NOVARTIS

TAF MEK Lung cancer - Safety profile - HCP

Prescribing information

Image

Image

Safety profile of TAFINLAR® (dabrafenib) + MEKINIST® (trametinib)

TAFINLAR in combination with MEKINIST is indicated in adult patients with advanced non-small cell lung cancer (NSCLC) with a *BRAF* V600 mutation.[1,2]

Common adverse events include:

- TAFINLAR + MEKINIST: The most common adverse reactions (incidence ≥ 20%) for dabrafenib in combination with trametinib were pyrexia, fatigue, nausea, chills, headache, diarrhoea, vomiting, arthralgia and rash[1,2]

- TAFINLAR: The most common adverse reactions (incidence >15%) reported with dabrafenib were hyperkeratosis, headache, pyrexia, arthralgia, fatigue, nausea, papilloma, alopecia, rash and vomiting[1]

- MEKINIST: The most common adverse reactions (incidence ≥20%) for trametinib were rash, diarrhoea, fatigue, oedema peripheral, nausea and dermatitis acneiform[2]

For the full safety profile, please refer to the Summary of Product Characteristics (SmPC) for TAFINLAR and MEKINIST.

Adverse event reporting: Details of how to report adverse events are available at the bottom of the page. Please refer to the respective SmPC for all licensed indications.

TAFINLAR + MEKINIST has a generally well-established safety profile[1–8]

The safety profile of Tafinlar + Mekinist in patients with *BRAF* V600-positive NSCLC is generally manageable and similar to that observed in adult patients with unresectable or metastatic melanoma with a *BRAF* V600 mutation.[6–8]

- Adverse reactions in the SmPC
- Contraindications/Precautions
- Managing pyrexia

Adverse reactions reported in the integrated safety population of TAFINLAR + MEKINIST in the studies MEK115306, MEK116513, BRF113928, and BRF115532 (n=1076)[1,2]

The corresponding frequency for each adverse drug reaction is based on the following: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1000 to <1/100); rare (≥1/10,000 to <1/1000); very rare (<1/10,000).[1,2]

System organ class	Frequency (all grades)	Adverse reactions

Infections and infestations	Very common	Nasopharyngitis
	Common	Urinary tract infection
		Cellulitis
		Folliculitis
		Paronychia
		Rash pustular
Neoplasms benign, malignant and unspecified (incl. cysts and polyps)	Common	Cutaneous squamous cell carcinoma*
		Papilloma[†]
		Seborrhoeic keratosis
	Uncommon	New primary melanoma[‡]
		Acrochordon (skin tags)
Blood and lymphatic system disorders	Common	Neutropenia
		Anaemia
		Thrombocytopenia
		Leukopenia
Immune system disorders	Uncommon	Hypersensitivity[§]
		Sarcoidosis
	Rare	Haemophagocytic lymphohistiocytosis
Metabolism and nutrition disorders	Very common	Decreased appetite
	Common	Dehydration
		Hyponatraemia
		Hypophosphataemia
		Hyperglycaemia
	Not known	Tumour lysis syndrome
Nervous system disorders	Very common	Headache
		Dizziness
	Common	Peripheral neuropathy (including sensory and motor neuropathy)
Eye disorders	Common	Vision blurred
		Visual impairment
		Uveitis
		Chorioretinopathy
	Uncommon	Retinal detachment
		Periorbital oedema

Cardiac disorders	Common	Ejection fraction decreased
	Uncommon	Bradycardia
		Atrioventricular block[¶]
	Not known	Myocarditis
Vascular disorders	Very common	Hypertension
		Haemorrhage[‖]
	Common	Hypotension
		Lymphoedema
Respiratory, thoracic and mediastinal disorders	Very common	Cough
	Common	Dyspnoea
	Uncommon	Pneumonitis
Gastrointestinal disorders	Very common	Abdominal pain**
		Constipation
		Diarrhoea
		Nausea
		Vomiting
	Common	Dry mouth
		Stomatitis
	Uncommon	Pancreatitis
		Colitis
	Rare	Gastrointestinal perforation

Skin and subcutaneous disorders	Very common	Dry skin
		Pruritus
		Rash
		Erythema[††]
	Common	Dermatitis acneiform
		Actinic keratosis
		Night sweats
		Hyperkeratosis
		Alopecia
		Palmar-plantar erythrodysaesthesia syndrome
		Skin lesion
		Hyperhidrosis
		Panniculitis
		Skin fissures
		Photosensitivity
	Uncommon	Acute febrile neutrophilic dermatosis
		Stevens-Johnson syndrome
	Not known	Drug reaction with eosinophilia and systemic symptoms
		Dermatitis exfoliative generalised
Musculoskeletal and connective tissue disorders	Very common	Arthralgia
		Muscle spasms[‡‡]
		Pain in extremity
		Myalgia
Renal and urinary disorders	Uncommon	Renal failure
		Nephritis
General disorders and administration-site conditions	Very common	Fatigue
		Chills
		Asthenia
		Oedema peripheral
		Pyrexia
	Common	Influenza-like illness
		Mucosal inflammation
		Face oedema

Investigations	Very common	Alanine aminotransferase increased
		Aspartate aminotransferase increased
		Blood alkaline phosphatase increased
	Common	Blood creatine phosphokinase increased
		Gamma-glutamyltransferase increased

Table adapted from TAFINLAR and MEKINIST SmPCs.[1,2]

The most common adverse reactions (incidence ≥20%) for TAFINLAR + MEKINIST were: pyrexia, fatigue, nausea, chills, headache, diarrhoea, vomiting, arthralgia and rash.

Contraindications

TAFINLAR contraindications: Hypersensitivity to the active substance or to the following excipients: microcrystalline cellulose, magnesium stearate, colloidal silicone dioxide, red iron oxide (E172), titanium dioxide (E171), hypromellose (E464), black iron oxide (E172), shellac, propylene glycol.[1]

MEKINIST contraindications: Hypersensitivity to the active substance or to the following excipients: mannitol (E421), microcrystalline cellulose (E460), hypromellose (E464), croscarmellose sodium (E468), magnesium stearate (E470b), sodium laurilsulfate, colloidal silicon dioxide (E551), titanium dioxide (E171), polyethylene glycol, iron oxide yellow (E172), polysorbate 80 (E433) and iron oxide red (E172).[2]

Special populations[1]

Elderly

Patients ≥65 years were more likely to experience adverse reactions leading to permanent discontinuation of the medicinal product, dose reduction, and dose interruption than those <65 years. Please refer to the SmPCs for further information about the safety profile in elderly populations.

TAFINLAR + MEKINIST in patients with brain metastases

The safety and efficacy of the combination of TAFLINLAR + MEKINIST have been evaluated in a multi-cohort, open-label, Phase II study in patients with *BRAF* V600 mutant melanoma with brain metastases. The safety profile observed in these patients appears to be consistent with the integrated safety profile of the combination.

Special warnings and precautions for use[1,2]

When TAFINLAR is given in combination with MEKINIST, the SmPC of TAFINLAR and MEKINIST must be consulted prior to initiation of combination treatment. For additional information on warnings and precautions associated with treatment, please refer to the respective SmPC.

BRAF V600 testing
The efficacy and safety of TAFINLAR + MEKINIST has not been evaluated in patients whose melanoma tested negative for the *BRAF* V600 mutation. TAFINLAR should not be used in patients with wild-type *BRAF* melanoma and NSCLC.

TAFINLAR + MEKINIST in patients with melanoma who have progressed on a _BRAF_ inhibitor
There are limited data in patients taking the combination of TAFINLAR + MEKINIST who have progressed on a prior *BRAF* inhibitor. These data show that the efficacy of the combination will be lower in these patients. Therefore, other treatment options should be considered before treatment with the combination in this prior *BRAF* inhibitor treated population. The sequencing of treatments following progression on a *BRAF* inhibitor therapy has not been established.

New malignancies
New malignancies, cutaneous and non-cutaneous, can occur with TAFINLAR + MEKINIST.

Cutaneous malignancies
Cutaneous squamous cell carcinoma (cuSCC)
Cases of cuSCC (including keratoacanthoma) have been reported in patients treated with TAFINLAR + MEKINIST. In the integrated safety population of patients with melanoma and advanced NSCLC, cuSCC occurred in 2% (19/1076) of patients receiving TAFINLAR + MEKINIST. The median time to diagnosis of the first occurrence of cuSCC in study MEK115306 was 223 days (range 56 to 510 days) in the combination therapy arm and 60 days (range 9 to 653 days) in the TAFINLAR monotherapy arm. In the Phase III study BRF115532 (COMBI-AD) in the adjuvant treatment of melanoma, 1% (6/435) of patients receiving TAFINLAR + MEKINIST as compared to 1% (5/432) of patients receiving placebo developed cuSCC. The median time to onset of the first occurrence of cuSCC in the combination arm of the adjuvant treatment study was approximately 18 weeks and was 33 weeks in the placebo arm.

It is recommended that skin examination be performed prior to initiation of therapy with dabrafenib and monthly throughout treatment and for up to six months after treatment for cuSCC. Monitoring should continue for 6 months following discontinuation or until initiation of another anti-neoplastic therapy.

Cases of cuSCC should be managed by dermatological excision and TAFINLAR treatment or, if taken in combination, TAFINLAR + MEKINIST should be continued without any dose adjustment. Patients should be instructed to immediately inform their physician if new lesions develop.

New primary melanoma
New primary melanoma was reported in patients receiving TAFINLAR + MEKINIST. Cases of new primary melanoma can be managed with excision and do not require treatment modification. Monitoring for skin lesions should occur as described for cuSCC.

Non-cutaneous malignancies
In vitro experiments have demonstrated paradoxical activation of mitogen-activated protein kinase (MAP kinase) signalling in *BRAF* wild-type cells with RAS mutations when exposed to *BRAF* inhibitors. This may lead to increased risk of non-cutaneous

malignancies with dabrafenib exposure when RAS mutations are present. RAS-associated malignancies have been reported in clinical trials with TAFINLAR + MEKINIST (colorectal cancer, pancreatic cancer).

Prior to initiation of treatment, patients should undergo a head and neck examination with minimally visual inspection of oral mucosa and lymph node palpation, as well as chest/abdomen computerised tomography (CT) scan. During treatment, patients should be monitored as clinically appropriate which may include a head and neck examination every 3 months and a chest/abdomen CT scan every 6 months. Anal examinations and pelvic examinations are recommended before and at the end of treatment or when considered clinically indicated. Complete blood cell counts and blood chemistry should be performed as clinically indicated.

The benefits and risks should be considered before administering TAFINLAR in patients with a prior or concurrent cancer associated with RAS mutations. No dose modification of trametinib is required with TAFINLAR + MEKINIST.

Following discontinuation of TAFINLAR, monitoring for non-cutaneous secondary/recurrent malignancies should continue for up to 6 months or until initiation of another anti-neoplastic therapy. Abnormal findings should be managed according to clinical practices.

Haemorrhage
Haemorrhagic events, including major haemorrhagic and fatal haemorrhages, have occurred in patients taking TAFINLAR + MEKINIST. The potential for these events in patients with low platelet counts (<75,000) has not been established, as such patients were excluded from clinical trials. The risk of haemorrhage may be increased with concomitant use of antiplatelet or anticoagulant therapy. If haemorrhage occurs, patients should be treated as clinically indicated.

Visual impairment
In clinical trials ophthalmologic reactions, including uveitis, iridocyclitis and iritis, have been reported in patients treated with TAFINLAR + MEKINIST. Patients should be routinely monitored for visual signs and symptoms (such as change in vision, photophobia and eye pain) while on therapy. MEKINIST is not recommended in patients with a history of retinal vein occlusion (RVO). The safety of MEKINIST in subjects with predisposing factors for RVO, including uncontrolled glaucoma or ocular hypertension, uncontrolled hypertension, uncontrolled diabetes mellitus, or a history of hyperviscosity or hypercoagulability syndromes, has not been established. In patients who are diagnosed with RVO, treatment with MEKINIST should be permanently discontinued.

No dose modifications are required as long as effective local therapies can control ocular inflammation. If uveitis does not respond to local ocular therapy, withhold dabrafenib until resolution of ocular inflammation and then restart dabrafenib reduced by one dose level. No dose modification of TAFINLAR is required when taken in combination with MEKINIST following diagnosis of uveitis.

Retinal pigment epithelial dystrophy (RPED) and RVO may occur with TAFINLAR + MEKINIST. No dose modification of TAFINLAR is required when taken in combination with MEKINIST following diagnosis of RVO or RPED.

Pyrexia
Fever has been reported in clinical trials with TAFINLAR + MEKINIST.

The incidence and severity of pyrexia are increased with combination therapy. In the combination therapy arm of study MEK115306 in patients with unresectable or metastatic melanoma, pyrexia was reported in 57% (119/209) of patients with 7% Grade 3, as compared to the TAFINLAR monotherapy arm with 33% (69/211) of patients reporting pyrexia, 2% Grade 3. In the Phase II study BRF113928 in patients with advanced NSCLC, the incidence and severity of pyrexia were increased slightly when TAFINLAR was used in combination with MEKINIST (48%, 3% Grade 3) as compared to dabrafenib monotherapy (39%, 2% Grade 3). In the Phase III study BRF115532 in the adjuvant treatment of melanoma, the incidence and severity of pyrexia were higher in the TAFINLAR + MEKINIST arm (67%; 6% Grade 3/4) as compared to the placebo arm (15%; <1% Grade 3).

For patients with unresectable or metastatic melanoma who received TAFINLAR + MEKINIST and developed pyrexia, approximately half of the first occurrences of pyrexia happened within the first month of therapy and approximately one-third of the patients had 3 or more events.

Therapy should be interrupted if the patient's temperature is ≥38°C. In case of recurrence, therapy can also be interrupted at the first symptom of pyrexia. Treatment with anti-pyretics such as ibuprofen or acetaminophen/paracetamol should be initiated. The use of oral corticosteroids should be considered in those instances in which anti-pyretics are insufficient. Patients should be evaluated for signs and symptoms of infection. When used as monotherapy, or both TAFINLAR and MEKINIST when used in combination, should be restarted if the patient is symptom-free for at least 24 hours either (1) at the same dose level, or (2) reduced by one dose level if pyrexia is recurrent and/or was accompanied by other severe symptoms including dehydration, hypotension or renal failure. Please see individual SmPCs for further information.

Left ventricular ejection fraction (LVEF) reduction/Left ventricular dysfunction
TAFINLAR + MEKINIST has been reported to decrease LVEF. No dose modification of TAFINLAR is required when taken in combination with MEKINIST. In patients receiving TAFINLAR in combination with MEKINIST, there have been occasional reports of acute, severe left ventricular dysfunction due to myocarditis. Full recovery was observed when stopping treatment. Physicians should be alert to the possibility of myocarditis in patients who develop new or worsening cardiac signs or symptoms. Trametinib should be used with caution in patients with impaired left ventricular function. Patients with left ventricular dysfunction, New York Heart Association Class II, III, or IV heart failure, acute coronary syndrome within the past 6 months, clinically significant uncontrolled arrhythmias, and uncontrolled hypertension were excluded from clinical trials; safety of use in this population is therefore unknown. LVEF should be evaluated in all patients prior to initiation of treatment with trametinib, one month after initiation of therapy, and then at approximately 3-monthly intervals while on treatment.

Renal failure
Renal failure has been identified in ≤1% of patients treated with TAFINLAR + MEKINIST. Observed cases were generally associated with pyrexia and dehydration and responded well to dose interruption and general supportive measures.

Granulomatous nephritis has been reported. Patients should be routinely monitored for serum creatinine while on therapy. If creatinine increases, TAFINLAR may need to be interrupted as clinically appropriate. TAFINLAR has not been studied in patients with renal insufficiency (defined as creatinine >1.5 x upper limit of normal), therefore caution should be used in this setting.

Hepatic events
Hepatic adverse events have been reported in clinical trials with TAFINLAR + MEKINIST. It is recommended that patients receiving treatment with TAFINLAR + MEKINIST have liver function monitored every 4 weeks for 6 months after treatment initiation with trametinib. Liver monitoring may be continued thereafter as clinically indicated.

Hypertension
Elevations in blood pressure have been reported in association with TAFINLAR + MEKINIST, in patients with or without pre-existing hypertension. Blood pressure should be measured at baseline and monitored during treatment with MEKINIST, with control of hypertension by standard therapy as appropriate.

Interstitial lung disease (ILD)/Pneumonitis
Cases of pneumonitis or ILD have been reported in clinical trials with TAFINLAR + MEKINIST. MEKINIST should be withheld in patients with suspected ILD or pneumonitis, including patients presenting with new or progressive pulmonary symptoms and findings including cough, dyspnoea, hypoxia, pleural effusion, or infiltrates, pending clinical investigations. MEKINIST should be permanently discontinued for patients diagnosed with treatment-related ILD or pneumonitis. If TAFINLAR is being used in combination with MEKINIST then therapy with TAFINLAR may be continued at the same dose.

Rash
Rash has been observed in about 60% of patients in TAFINLAR monotherapy studies and about 24% of patients in clinical trials with TAFINLAR + MEKINIST. The majority of these cases were Grade 1 or 2 and did not require any dose interruptions or dose reductions.

Rhabdomyolysis
Rhabdomyolysis has been reported in patients taking TAFINLAR + MEKINIST. In some cases, patients were able to continue MEKINIST. In more severe cases, hospitalisation, interruption or permanent discontinuation of MEKINIST or TAFINLAR + MEKINIST was required. Signs or symptoms of rhabdomyolysis should warrant an appropriate clinical evaluation and treatment as indicated.

Pancreatitis
Pancreatitis has been reported in <1% of patients treated with TAFINLAR + MEKINIST in unresectable or metastatic melanoma clinical trials and about 4% of patients treated with TAFINLAR + MEKINIST in the NSCLC clinical trial. In the adjuvant treatment of melanoma trial, pancreatitis was reported in <1% (1/435) of patients receiving TAFINLAR + MEKINIST, and no patients receiving placebo. Unexplained abdominal pain should be promptly investigated to include measurement of serum amylase and lipase. Patients should be closely monitored when re-starting TAFINLAR after an episode of pancreatitis.

Deep vein thrombosis/Pulmonary embolism
Pulmonary embolism or deep vein thrombosis can occur with TAFINLAR + MEKINIST. If patients develop symptoms of pulmonary embolism or deep vein thrombosis such as shortness of breath, chest pain, or arm or leg swelling, they should immediately seek medical care. Permanently discontinue TAFINLAR + MEKINIST for life-threatening pulmonary embolism.

Severe cutaneous adverse reactions
Cases of severe cutaneous adverse reactions (SCARs), including Stevens-Johnson syndrome, and drug reaction with eosinophilia and systemic symptoms (DRESS), which can be life-threatening or fatal, have been reported during treatment with TAFINLAR + 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 + MEKINIST should be withdrawn.

Gastrointestinal disorders
Colitis and gastrointestinal perforation, including fatal outcome, have been reported in patients taking TAFINLAR + MEKINIST. Treatment with MEKINIST monotherapy or TAFINLAR + MEKINIST should be used with caution in patients with risk factors for gastrointestinal perforation, including history of diverticulitis, metastases to the gastrointestinal tract and concomitant use of medicinal products with a recognised risk of gastrointestinal perforation.

Sarcoidosis
Cases of sarcoidosis have been reported in patients treated with TAFINLAR + MEKINIST, mostly involving the skin, lung, eye and lymph nodes. In the majority of the cases, treatment with TAFINLAR + MEKINIST was maintained. In case of a diagnosis of sarcoidosis, relevant treatment should be considered. It is important not to misinterpret sarcoidosis as disease progression.

Haemophagocytic lymphohistiocytosis
In post-marketing experience, haemophagocytic lymphohistiocytosis (HLH) has been observed in patients treated with TAFINLAR + MEKINIST. Caution should be taken when MEKINIST is administered in combination with TAFINLAR. If HLH is confirmed, administration of TAFINLAR + MEKINIST should be discontinued and treatment for HLH initiated.

Sodium
MEKINIST contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially “sodium-free”.

Effects of other medicinal products on dabrafenib
TAFINLAR is a substrate of CYP2C8 and CYP3A4. Potent inducers of these enzymes should be avoided when possible, as these agents may decrease the efficacy of TAFINLAR.

In vivo and *in vitro* data suggest that the pharmacokinetics of MEKINIST are unlikely to be affected by other medicinal products. MEKINIST is not a substrate of CYP enzymes or of the transporters BCRP, OATP1B1, OATP1B3, OATP2B1, OCT1, MRP2, and MATE1. MEKINIST is an *in vitro* substrate of BSEP and the efflux transporter P-gp. Although MEKINIST exposure is unlikely to be affected by inhibition of BSEP, increased levels of MEKINIST upon strong inhibition of hepatic P-gp cannot be excluded.

Effects of dabrafenib on other medicinal products
TAFINLAR is an inducer of metabolising enzymes, which may lead to loss of efficacy of many commonly used medicinal products. A drug utilisation review (DUR) is therefore essential when initiating TAFINLAR treatment. Concomitant use of TAFINLAR with medicinal products that are sensitive substrates of certain metabolising enzymes or transporters should generally be avoided if monitoring for efficacy and dose adjustment is not possible.

Concomitant administration of TAFINLAR with warfarin results in decreased warfarin exposure. Caution should be exercised and additional International Normalised Ratio (INR) monitoring is recommended when TAFINLAR is used concomitantly with warfarin and at discontinuation of TAFINLAR.

Concomitant administration of TAFINLAR with digoxin may result in decreased digoxin exposure. Caution should be exercised and additional monitoring of digoxin is recommended when digoxin (a transporter substrate) is used concomitantly with TAFINLAR and at discontinuation of TAFINLAR.

The effect of repeat-dose MEKINIST on the steady state pharmacokinetics of combination oral contraceptives norethindrone and ethinyl estradiol was assessed in a clinical study that consisted of 19 female patients with solid tumours. Norethindrone exposure increased by 20% and ethinyl estradiol exposure was similar when co-administered with MEKINIST. Based on these results, no loss of efficacy of hormonal contraceptives is expected when co-administered with MEKINIST monotherapy.

Effect of other medicinal products on trametinib
As MEKINIST is metabolised predominantly via deacetylation mediated by hydrolytic enzymes (e.g. carboxyl-esterases), its pharmacokinetics are unlikely to be affected by other agents through metabolic interactions. Drug-drug interactions via these hydrolytic enzymes cannot be ruled out and could influence the exposure to MEKINIST.

MEKINIST is an *in vitro* substrate of the efflux transporter P-gp. As it cannot be excluded that strong inhibition of hepatic P-gp may result in increased levels of MEKINIST, caution is advised when co-administering MEKINIST with medicinal products that are strong inhibitors of P-gp (e.g. verapamil, cyclosporine, ritonavir, quinidine, itraconazole).

Effect of trametinib on other medicinal products
Based on *in vitro* and *in vivo* data, MEKINIST is unlikely to significantly affect the pharmacokinetics of other medicinal products via interaction with CYP enzymes or transporters. MEKINIST may result in transient inhibition of BCRP substrates (e.g. pitavastatin) in the gut, which may be minimised with staggered dosing (2 hours apart) of these agents and MEKINIST.

Based on clinical data, no loss of efficacy of hormonal contraceptives is expected when co-administered with MEKINIST monotherapy.

- Across clinical trials, pyrexia was the most common adverse event observed in patients treated with TAFINLAR + MEKINIST[1–8]

- Most pyrexia events were mild or moderate (Grade 1/2)[4,5,9]
- Therapy with TAFINLAR + MEKINIST should be interrupted if the patient's temperate is ≥38 °C[1,2]
- In case of recurrence, therapy can also be interrupted at the first symptom of pyrexia[1,2]
- Patients may respond well to dose interruption and/or dose reduction and supportive care for the management of pyrexia, allowing re-initiation of treatment[1,2]

Three-step guidance for managing pyrexia (≥38 °C)[1,2]

1. Interrupt	2. Manage	3. Restart
◦ Interrupt TAFINLAR + MEKINIST	◦ Evaluate for infection and, if necessary, treat in accordance with local practice ◦ Initiate antipyretics such as ibuprofen or paracetamol ◦ Consider oral corticosteroids in instances in which antipyretics are insufficient	If the patient is symptom free for at least 24 hours, restart TAFINLAR + MEKINIST either: ◦ At the same dosage OR ◦ At a reduced dosage if the pyrexia was recurrent and/or was accompanied by other severe signs and symptoms

Advice for healthcare professionals (HCPs) and patients

Image

Advice for HCPs

Image

Rule out infective cause

Image

Check blood pressure and carry out a full blood count to rule out neutropenia

Image

If antifungal or antibiotic therapy is required, please refer to the SmPCs, as some products may interact with TAFINLAR

Image

Some patients may also have hypotension or general malaise and need to be hospitalised

Image

Advice for your patients

Image

Drink plenty of non-alcoholic and caffeine-free fluids to prevent dehydration

Image

A lukewarm bath, an ice pack or cool, moist flannel on the forehead or back of the neck can make you feel more comfortable

Image

Take appropriate medication as prescribed to control your fever

Image

In case of hospitalisation due to pyrexia, inform the healthcare professional treating you that you are on TAFINLAR + MEKINIST, which causes pyrexia as a common side effect

Accompanying symptoms: pyrexia may be accompanied by severe rigors, dehydration and hypotension, which in some cases can lead to acute renal insufficiency.

*Cutaneous squamous cell carcinoma (cuSCC): SCC, SCC of the skin, SCC in situ (Bowen's disease) and keratoacanthoma.
†Papilloma, skin papilloma.
‡Malignant melanoma, metastatic malignant melanoma, and superficial spreading melanoma Stage III.
§Includes drug hypersensitivity.
¶Including atrioventricular block complete.
‖Bleeding from various sites, including intracranial bleeding and fatal bleeding.
**Abdominal pain upper and abdominal pain lower.
††Erythema, generalised erythema.
‡‡Muscle spasms, musculoskeletal stiffness.

BRAF V600, mutation of the *BRAF* gene at valine (V) 600; CT, computerised tomography; cuSCC, cutaneous squamous cell carcinoma; DRESS, drug reaction with eosinophilia and systemic symptoms; DUR, drug utilisation review; HCP, healthcare professional; HLH, haemophagocytic lymphohistiocytosis; ILD, interstitial lung disease; LVEF, left ventricular ejection fraction; MAP, mitogen-activated protein; NSCLC, non-small cell lung cancer; RPED, retinal pigment epithelial dystrophy; RVO, retinal vein occlusion; SCAR, severe cutaneous adverse reaction; SCC, squamous cell carcinoma; SmPC, summary of product characteristics.

References

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BRAF mutation and mechanism of action for TAFINLAR + MEKINIST

BRAF mutation and mechanism of action for TAFINLAR + MEKINIST

See more details

Hide details

Efficacy

Efficacy

See more details

Hide details

Dosing and administration

Dosing and administration

See more details

Hide details

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Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Novartis online through the pharmacovigilance intake (PVI) tool at www.novartis.com/report, or alternatively email medinfo.uk@novartis.com or call 01276 698370.
