אוקטובר 2024

רופא/ה נכבד/ה, רוקח/ת נכבד/ה,

שלום רב,

הנדון: עדכוני בטיחות בעלוני התכשיר -
Tafinlar 50 mg, 75 mg, Hard capsules

חברת נוברטיס ישראל בע"מ מבקשת להודיעכם על עדכון בעלון לרופא ובעלון לצרכן של התכשירים:
Tafinlar 50 mg & Tafinlar 75 mg

התוויות התכשיר:

Melanoma
Dabrafenib as monotherapy or in combination with trametinib is indicated for the treatment of adult patients with unresectable or metastatic melanoma with a BRAF V600 mutation.
Adjuvant treatment of melanoma
Dabrafenib in combination with trametinib is indicated for the adjuvant treatment of adult patients with Stage III melanoma with a BRAF V600 mutation, following complete resection.
Non-small cell lung cancer (NSCLC)
Dabrafenib in combination with trametinib is indicated for the treatment of adult patients with advanced non-small cell lung cancer with a BRAF V600 mutation.
Anaplastic Thyroid Cancer (ATC)
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.
BRAF V600E Mutation-Positive Low-Grade Glioma
Dabrafenib is indicated, in combination with trametinib, for the treatment of pediatric patients 6 year of age and older with low-grade glioma (LGG) with a BRAF V600E mutation who require systemic therapy.

חומר פעיל: DABRAFENIB (AS MESILATE) 50mg, 75mg

בהודעה זו מפורטים העדכונים המהווים עדכונים מהותיים בלבד. למידע מלא יש לעיין בעלוני התכשיר.
(טקסט שנוסף מסומן בצבע עם קו תחתי, טקסט שהוסר מסומן בצבע ובקו חצייה ,שינויים אשר מהווים מידע בטיחות חדש מסומנים ברקע צהוב)

העלונים נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלם מודפסים על-ידי פניה לבעל הרישום:
נוברטיס ישראל בע"מ. תוצרת הארץ 6, ת.ד. 7126, תל אביב

בברכה,

ניב טובי
רוקח ממונה

Novartis Israel Ltd.
P.O.Box 7126 6 Tozeret Haaretz street, Tel Aviv
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4.4 Special warnings and precautions for use

[…]

Cutaneous squamous cell carcinoma (cuSCC)

Cases of cuSCC (including keratoacanthoma) have been reported in patients treated with dabrafenib alone and in combination with trametinib (see section 4.8). In the Phase III clinical trials MEK115306 and MEK116513 in patients with unresectable or metastatic melanoma, cuSCC occurred in 10% (22/211) of patients receiving dabrafenib as a monotherapy and in 18% (63/349) of patients receiving vemurafenib as a monotherapy, respectively. In the integrated safety population of patients with melanoma and advanced NSCLC, cuSCC occurred in 2% (19/1076) of patients receiving dabrafenib in combination with trametinib. 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 dabrafenib monotherapy arm. In the Phase III study BRF115532 (COMBI-AD) in the adjuvant treatment of melanoma, 1% (6/435) of patients receiving dabrafenib in combination with trametinib as compared to 1% (5/432) of patients receiving placebo had developed cuSCC at the time of the primary analysis. During the long-term (up to 10 years) off-treatment follow-up, 2 additional patients reported cuSCC in each treatment arm. Overall, ~~T~~the median time to onset of the first occurrence of cuSCC in the combination arm of the adjuvant treatment study was approximately 218 weeks and was ~~33~~ 34 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 of dabrafenib or until initiation of another anti-neoplastic therapy.

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

4.8 Undesirable effects

[…]

Table 5. Adverse reactions with dabrafenib monotherapy

System organ class	Frequency (all grades)	Adverse reactions
[…]		
Skin and subcutaneous tissue disorders	Very common	Hyperkeratosis
		Alopecia
		Rash
		Palmar –plantar erythrodysaesthesia syndrome
	Common	Dry skin
		Pruritus
		Actinic keratosis
		Skin lesion
		Erythema
		Photosensitivity
	Uncommon	Acute febrile neutrophilic dermatosis
		Panniculitis

[…]

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Table 6. Adverse reactions with dabrafenib in combination with trametinib

System organ class	Frequency (all grades)	Adverse reactions
[…]		
Skin and subcutaneous tissue disorders	Very common	Dry skin
		Pruritus
		Rash
		Erythema[h]
	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
	Not known	Stevens-Johnson syndrome
		Drug reaction with eosinophilia and systemic symptoms
		Dermatitis exfoliative generalised

[…]

Non-cutaneous malignancy

Activation of MAP kinase signalling in BRAF wild-type cells which are exposed to BRAF inhibitors may lead to increased risk of non-cutaneous malignancies, including those with RAS mutations (see section 4.4). Non-cutaneous malignancies were reported in 1% (6/586) of patients in the integrated safety population of dabrafenib monotherapy, and <1% (8/1076) of patients in the integrated safety population of dabrafenib in combination with trametinib. In the Phase III study BRF115532 (COMBI-AD) in the adjuvant treatment of melanoma, 1% (5/435) of patients receiving dabrafenib in combination with trametinib as compared to <1% (3/432) of patients receiving placebo developed non-cutaneous malignancies. During the long-term (up to 10 years) off-treatment follow-up, 9 additional patients reported non-cutaneous malignancies in the combination arm and 4 in in the placebo arm. Cases of RAS-driven malignancies have been seen with dabrafenib as monotherapy and in combination with trametinib. Patients should be monitored as clinically appropriate.

[…]

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עדכונים מהותיים בעלון לצרכן

4. תופעות לוואי

[...]

תופעות הלוואי שאתה עלול לחוות כשאתה לוקח טפינלר כטיפול יחיד הן:
[...]

תופעות לוואי לא שכיחות (עלולות להופיע ב-1-10 משתמשים מתוך 1,000):
[...]

- כתמי עור או פצעים מורמים, כואבים, אדומים עד אדמדמים-סגולים כהים, המופיעים בעיקר על הידיים, הרגליים, הפנים והצוואר, מלווים בחום (סימנים של דרמטוזיס נויטרופילי חריף – acute febrile neutrophilic dermatosis)

תופעות הלוואי האחרות שאתה עלול להבחין בהן כאשר אתה לוקח טפינלר בשילוב עם טרמטיניב הן אלו:
[...]

תופעות לוואי לא שכיחות (עלולות להופיע ב-1-10 משתמשים מתוך 1,000):
[...]
- כתמי עור או פצעים מורמים, כואבים, אדומים עד אדמדמים-סגולים כהים, המופיעים בעיקר על הידיים, הרגליים, הפנים והצוואר, מלווים בחום (סימנים של דרמטוזיס נויטרופילי חריף – acute febrile neutrophilic dermatosis)

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