

נובמבר 2021

רופא/ה נכבד/ה, רוקח/ת נכבד/ה,

**הנדון: הודעה לצוות הרפואי על עדכוני בטיחות בעלוני התכשיר**

**Votrient 200 mg (33192) and 400 mg (33194) FCT**

**וטריוינט 200 ו- 400 מ"ג**

חברת נוברטיס ישראל בע"מ מבקשת להודיע על עדכון בעלון לצרכן ועלון לרופא של התכשיר .Votrient 200mg/400mg. בהודעה זו מפורטים העדכונים המהווים החמרה במידע הבטיחותי בלבד. למידע מלא יש לעיין בעלוני התכשיר. 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  
טלפון: 03-92011110

**התוויה כפי שאושרה בתעודת הרישום:**

**Renal cell carcinoma (RCC)**

Votrient is indicated in adults for the first line treatment of advanced Renal Cell Carcinoma (RCC) and for patients who have received prior cytokine therapy for advanced disease.

**Soft tissue sarcoma (STS)**

Votrient is indicated for the treatment of adult patients with selective subtypes of advanced Soft Tissue Sarcoma (STS) who have received prior chemotherapy for metastatic disease or who have progressed within 12 months after (neo) adjuvant therapy.

PAZOPANIB (AS HYDROCHLORIDE)

**חומר פעיל:**

העלונים לרופא ולצרכן עודכנו בספטמבר 2021. להלן העדכונים המהווים החמרה במידע הבטיחותי ( מסומנים בצהוב):

Novartis Israel Ltd.  
6 Tozeret Haaretz street, Tel Aviv P.O.Box 7126  
Tel: 972-3-9201111 Fax: 972-3-9229331

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טלפון: 9201111-03 פקס: 922-03-9331

**4.4 Special warnings and precautions for use**

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Combination with other systemic anti-cancer therapies

Clinical studies of pazopanib in combination with a **number of other anti-cancer therapies (including for example** pemetrexed, (non-small cell lung cancer [NSCLC]) and lapatinib **or pembrolizumab** (cervical cancer) were terminated early due to concerns over increased toxicity and/or mortality, and a safe and effective combination dose has not been established with these regimens.

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**4.8 Undesirable effects**

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**Table 3 Treatment-related adverse reactions reported in STS studies (n=382) or during post-marketing period**

System Organ Class	Frequency (all grades)	Adverse reactions	All grades n (%)	Grade 3 n (%)	Grade 4 n (%)
Infections and infestations	Common	Gingival infection	4 (1%)	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Very common	Tumour pain	121 (32%)	32 (8%)	0
Blood and lymphatic system disorders <sup>f</sup>	Very common	Leukopenia	106 (44%)	3 (1%)	0
		Thrombocytopenia	86 (36%)	7 (3%)	2 (<1%)
		Neutropenia	79 (33%)	10 (4%)	0
	Uncommon	Thrombotic microangiopathy (including thrombotic thrombocytopenic purpura and haemolytic uraemic syndrome)	1 (<1%)	1 (<1%)	0
Endocrine disorders	Common	Hypothyroidism	18 (5%)	0	0
Metabolism and	Very common	Decreased appetite	108 (28%)	12 (3%)	0

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<b>nutrition disorders</b>		<b>Hypoalbuminemia<sup>f</sup></b>	<b>81 (34%)</b>	<b>2 (&lt;1%)</b>	<b>0</b>
	<b>Common</b>	<b>Dehydration</b>	<b>4 (1%)</b>	<b>2 (1%)</b>	<b>0</b>
	<b>Uncommon</b>	<b>Hypomagnesaemia</b>	<b>1 (&lt;1%)</b>	<b>0</b>	<b>0</b>
	<b>Not known</b>	<b>Tumour lysis syndrome*</b>	<b>not known</b>	<b>not known</b>	<b>not known</b>
<b>Psychiatric disorders</b>	<b>Common</b>	<b>Insomnia</b>	<b>5 (1%)</b>	<b>1 (&lt;1%)</b>	<b>0</b>
<b>Nervous system disorders</b>	<b>Very common</b>	<b>Dysgeusia<sup>c</sup></b>	<b>79 (21%)</b>	<b>0</b>	<b>0</b>
		<b>Headache</b>	<b>54 (14%)</b>	<b>2 (&lt;1%)</b>	<b>0</b>
	<b>Common</b>	<b>Peripheral sensory neuropathy</b>	<b>30 (8%)</b>	<b>1 (&lt;1%)</b>	<b>0</b>
		<b>Dizziness</b>	<b>15 (4%)</b>	<b>0</b>	<b>0</b>
	<b>Uncommon</b>	<b>Somnolence</b>	<b>3 (&lt;1%)</b>	<b>0</b>	<b>0</b>
		<b>Paresthesia</b>	<b>1 (&lt;1%)</b>	<b>0</b>	<b>0</b>
		<b>Cerebral infarction</b>	<b>1 (&lt;1%)</b>	<b>0</b>	<b>1 (&lt;1%)</b>
<b>Eye disorders</b>	<b>Common</b>	<b>Vision blurred</b>	<b>15 (4%)</b>	<b>0</b>	<b>0</b>
<b>Cardiac disorders</b>	<b>Common</b>	<b>Cardiac dysfunction<sup>g</sup></b>	<b>21 (5%)</b>	<b>3 (&lt;1%)</b>	<b>1 (&lt;1%)</b>
		<b>Left ventricular dysfunction</b>	<b>13 (3%)</b>	<b>3 (&lt;1%)</b>	<b>0</b>
		<b>Bradycardia</b>	<b>4 (1%)</b>	<b>0</b>	<b>0</b>
	<b>Uncommon</b>	<b>Myocardial infarction</b>	<b>1 (&lt;1%)</b>	<b>0</b>	<b>0</b>
<b>Vascular disorders</b>	<b>Very common</b>	<b>Hypertension</b>	<b>152 (40%)</b>	<b>26 (7%)</b>	<b>0</b>
	<b>Common</b>	<b>Venous thromboembolic event<sup>d</sup></b>	<b>13 (3%)</b>	<b>4 (1%)</b>	<b>5 (1%)</b>
		<b>Hot flush</b>	<b>12 (3%)</b>	<b>0</b>	<b>0</b>
		<b>Flushing</b>	<b>4 (1%)</b>	<b>0</b>	<b>0</b>
	<b>Uncommon</b>	<b>Haemorrhage</b>	<b>2 (&lt;1%)</b>	<b>1 (&lt;1%)</b>	<b>0</b>
	<b>Not known</b>	<b>Aneurysms and artery dissections</b>	<b>not known</b>	<b>not known</b>	<b>not known</b>
<b>Respiratory,</b>	<b>Common</b>	<b>Epistaxis</b>	<b>22 (6%)</b>	<b>0</b>	<b>0</b>

thoracic and mediastinal disorders		Dysphonia	20 (5%)	0	0	
		Dyspnoea	14 (4%)	3 (<1%)	0	
		Cough	12 (3%)	0	0	
		Pneumothorax	7 (2%)	2 (<1%)	1 (<1%)	
		Hiccups	4 (1%)	0	0	
		Pulmonary haemorrhage	4 (1%)	1 (<1%)	0	
	Uncommon		Oropharyngeal pain	3 (<1%)	0	0
			Bronchial haemorrhage	2 (<1%)	0	0
			Rhinorrhoea	1 (<1%)	0	0
			Haemoptysis	1 (<1%)	0	0
Rare		Interstitial lung disease/pneumonitis †	not known	not known	not known	
Gastrointestinal disorders	Very common	Diarrhoea	174 (46%)	17 (4%)	0	
		Nausea	167 (44%)	8 (2%)	0	
		Vomiting	96 (25%)	7 (2%)	0	
		Abdominal pain <sup>a</sup>	55 (14%)	4 (1%)	0	
		Stomatitis	41 (11%)	1 (<1%)	0	
	Common	Abdominal distension	16 (4%)	2 (1%)	0	
		Dry mouth	14 (4%)	0	0	
		Dyspepsia	12 (3%)	0	0	
		Mouth haemorrhage	5 (1%)	0	0	
		Flatulence	5 (1%)	0	0	
		Anal haemorrhage	4 (1%)	0	0	
	Uncommon	Gastrointestinal haemorrhage	2 (<1%)	0	0	
		Rectal haemorrhage	2 (<1%)	0	0	

		Enterocutaneous fistula	1 (<1%)	1 (<1%)	0
		Gastric haemorrhage	1 (<1%)	0	0
		Melaena	2 (<1%)	0	0
		Oesophageal haemorrhage	1 (<1%)	0	1 (<1%)
		Peritonitis	1 (<1%)	0	0
		Retroperitoneal haemorrhage	1 (<1%)	0	0
		Upper gastrointestinal haemorrhage	1 (<1%)	1 (<1%)	0
		Ileal perforation	1 (<1%)	0	1 (<1%)
Hepatobiliary disorders	Uncommon	Hepatic function abnormal	2 (<1%)	0	1 (<1%)
	Not known	Hepatic failure*	not known	not known	not known
Skin and subcutaneous disorders	Very common	Hair colour change	93 (24%)	0	0
		Skin hypopigmentation	80 (21%)	0	0
		Exfoliative rash	52 (14%)	2 (<1%)	0
	Common	Alopecia	30 (8%)	0	0
		Skin disorder <sup>c</sup>	26 (7%)	4 (1%)	0
		Dry skin	21 (5%)	0	0
		Hyperhidrosis	18 (5%)	0	0
		Nail disorder	13 (3%)	0	0
		Pruritus	11 (3%)	0	0
		Erythema	4 (1%)	0	0
	Uncommon	Skin ulcer	3 (<1%)	1 (<1%)	0
		Rash	1 (<1%)	0	0
		Rash papular	1 (<1%)	0	0

		Photosensitivity reaction	1 (<1%)	0	0
		Palmar-plantar erythrodysesthesia syndrome	2 (<1%)	0	0
Musculoskeletal and connective tissue disorders	Common	Musculoskeletal pain	35 (9%)	2 (<1%)	0
		Myalgia	28 (7%)	2 (<1%)	0
		Muscle spasms	8 (2%)	0	0
	Uncommon	Arthralgia	2 (<1%)	0	0
Renal and urinary disorders	Uncommon	Proteinuria	2 (<1%)	0	0
Reproductive system and breast disorder	Uncommon	Vaginal haemorrhage	3 (<1%)	0	0
		Menorrhagia	1 (<1%)	0	0
General disorders and administration site conditions	Very common	Fatigue	178 (47%)	34 (9%)	1 (<1%)
	Common	Oedema <sup>b</sup>	18 (5%)	1 (<1%)	0
		Chest pain	12 (3%)	4 (1%)	0
		Chills	10 (3%)	0	0
	Uncommon	Mucosal inflammation <sup>e</sup>	1 (<1%)	0	0
Asthenia		1 (<1%)	0	0	
Investigations <sup>h</sup>	Very common	Weight decreased	86 (23%)	5 (1%)	0
	Common	Ear, nose and throat examination abnormal <sup>e</sup>	29 (8%)	4 (1%)	0
		Alanine aminotransferase increased	8 (2%)	4 (1%)	2 (<1%)
		Blood cholesterol abnormal	6 (2%)	0	0
		Aspartate aminotransferase increased	5 (1%)	2 (<1%)	2 (<1%)

		<b>Gamma glutamyltransferase increased</b>	<b>4 (1%)</b>	<b>0</b>	<b>3 (&lt;1%)</b>
	<b>Uncommon</b>	<b>Blood bilirubin increased</b>	<b>2 (&lt;1%)</b>	<b>0</b>	<b>0</b>
		<b>Aspartate aminotransferase</b>	<b>2 (&lt;1%)</b>	<b>0</b>	<b>2 (&lt;1%)</b>
		<b>Alanine aminotransferase</b>	<b>1 (&lt;1%)</b>	<b>0</b>	<b>1 (&lt;1%)</b>
		<b>Platelet count decreased</b>	<b>1 (&lt;1%)</b>	<b>0</b>	<b>1 (&lt;1%)</b>
		<b>Electrocardiogram QT prolonged</b>	<b>2 (&lt;1%)</b>	<b>1 (&lt;1%)</b>	<b>0</b>

†Treatment-related adverse reaction reported during post-marketing period (spontaneous case reports and serious adverse reactions from all pazopanib clinical studies).

\*Treatment-related adverse reaction reported only during the post-marketing period. Frequency cannot be estimated from the available data.

The following terms have been combined:

<sup>a</sup> Abdominal pain, abdominal pain upper and gastrointestinal pain

<sup>b</sup> Oedema, oedema peripheral and eyelid oedema

<sup>c</sup> The majority of these cases were Palmar-plantar erythrodysesthesia syndrome

<sup>d</sup> Venous thromboembolic events – includes Deep vein thrombosis, Pulmonary embolism and Thrombosis terms

<sup>e</sup> The majority of these cases describe mucositis

<sup>f</sup> Frequency is based on laboratory value tables from VEG110727 (N=240). These were reported as adverse events less frequently by investigators than as indicated by laboratory value tables.

<sup>g</sup> Cardiac dysfunction events – includes Left ventricular dysfunction, Cardiac failure and Restrictive cardiomyopathy

<sup>h</sup> Frequency is based on adverse events reported by investigators. Laboratory abnormalities were reported as adverse events less frequently by investigators than as indicated by laboratory value tables.

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## 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antineoplastic agents, ~~other antineoplastic agents~~ protein kinase inhibitors, **other** protein kinase inhibitors, ATC code: **L01EX03**~~L01XE11~~

### 4. תופעות לוואי

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**תופעות לוואי ששכיחותן אינה ידועה** (תופעות שאת שכיחותן לא ניתן לאמוד מהנתונים הזמינים):

-הרחבה והחלשות של דופן כלי הדם או קרע בדופן כלי הדם (מפרצת ובתירת העורק- דיסקציה של העורק)  
-תסמונת פירוק הגידול כתוצאה מפירוק מהיר של תאי סרטן  
-**א' ספיקת כבד**

לתשומת לבכם, בנוסף למצוין לעיל, העלונים כוללים שינויי ניסוח קלים נוספים.

העלונים לרופא ולצרכן נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלם מודפסים על-ידי פניה לבעל הרישום.

בברכה,

יעל לוי טל

רוקחת ממונה

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