

הנדון: עדכון העלון לרופא והעלון לצרכן של התכשירים:

VOTRIENT 200 mg
VOTRIENT 400 mg

התכשירים שבנדון רשומים בישראל להתוויות הבאות:

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.

המרכיב הפעיל: PAZOPANIB (as Hydrochloride)

ברצוננו להודיעכם על עדכונים בעלון לרופא והעלון לצרכן של התכשירים בנדון.

העדכון הינו בפרק תופעות הלוואי ומפורט להלן:

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

אי ספיקת כבד

Tabulated list of adverse reactions

Table 2 Treatment-related adverse reactions reported in RCC studies (n = 1149) 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	Infections (with or without neutropenia) [†]	not known	not known	not known
	Uncommon	Gingival infection	1 (<1%)	0	0
		Infectious peritonitis	1 (<1%)	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Uncommon	Tumour pain	1 (<1%)	1 (<1%)	0
Blood and lymphatic system disorders	Common	Thrombocytopenia	80 (7%)	10 (<1%)	5 (<1%)
		Neutropenia	79 (7%)	20 (2%)	4 (<1%)
		Leukopenia	63 (5%)	5 (<1%)	0

	Uncommon	Polycythaemia	6 (0.03%)	1	0
	Rare	Thrombotic microangiopathy (including thrombotic thrombocytopenic purpura and haemolytic uraemic syndrome)†	not known	not known	not known
Endocrine disorders	Common	Hypothyroidism	83 (7%)	1 (<1%)	0
Metabolism and nutrition disorders	Very common	Decreased appetite ^e	317 (28%)	14 (1%)	0
	Common	Hypophosphataemia	21 (2%)	7 (<1%)	0
		Dehydration	16 (1%)	5 (<1%)	0
	Uncommon	Hypomagnesaemia	10 (<1%)	0	0
	Not known	Tumour lysis syndrome*	not known	not known	not known
Psychiatric disorders	Common	Insomnia	30 (3%)	0	0
Nervous system disorders	Very common	Dysgeusia ^c	254 (22%)	1 (<1%)	0
		Headache	122 (11%)	11 (<1%)	0
	Common	Dizziness	55 (5%)	3 (<1%)	1 (<1%)
		Lethargy	30 (3%)	3 (<1%)	0
		Paraesthesia	20 (2%)	2 (<1%)	0
		Peripheral sensory neuropathy	17 (1%)	0	0
	Uncommon	Hypoaesthesia	8 (<1%)	0	0
		Transient ischaemic attack	7 (<1%)	4 (<1%)	0
		Somnolence	3 (<1%)	1 (<1%)	0
		Cerebrovascular accident	2 (<1%)	1 (<1%)	1 (<1%)
		Ischaemic stroke	2 (<1%)	0	1 (<1%)
Rare	Posterior reversible encephalopathy/ reversible posterior leukoencephalopathy syndrome†	not known	not known	not known	
Eye disorders	Common	Vision blurred	19 (2%)	1 (<1%)	0
	Uncommon	Retinal detachment†	1 (<1%)	1 (<1%)	0
		Retinal tear†	1 (<1%)	1 (<1%)	0
		Eyelash discolouration	4 (<1%)	0	0
Cardiac disorders	Uncommon	Bradycardia	6 (<1%)	0	0
		Myocardial infarction	5 (<1%)	1 (<1%)	4 (<1%)
		Cardiac dysfunction ^f	4 (<1%)	1 (<1%)	0
		Myocardial ischaemia	3 (<1%)	1 (<1%)	0
Vascular disorders	Very common	Hypertension	473 (41%)	115 (10%)	1 (<1%)
	Common	Hot flush	16 (1%)	0	0
		Venous thromboembolic event ^g	13 (1%)	6 (<1%)	7 (<1%)
		Flushing	12 (1%)	0	0
	Uncommon	Hypertensive crisis	6 (<1%)	0	2 (<1%)
		Haemorrhage	1 (<1%)	0	0

	Not known	Aneurysms and artery dissections	not known	not known	not known
Respiratory, thoracic and mediastinal disorders	Common	Epistaxis	50 (4%)	1 (<1%)	0
		Dysphonia	48 (4%)	0	0
		Dyspnoea	42 (4%)	8 (<1%)	1 (<1%)
		Haemoptysis	15 (1%)	1 (<1%)	0
	Uncommon	Rhinorrhoea	8 (<1%)	0	0
		Pulmonary haemorrhage	2 (<1%)	0	0
		Pneumothorax	1 (<1%)	0	0
Rare	Interstitial lung disease/pneumonitis†	not known	not known	not known	
Gastrointestinal disorders	Very common	Diarrhoea	614 (53%)	65 (6%)	2 (<1%)
		Nausea	386 (34%)	14 (1%)	0
		Vomiting	225 (20%)	18 (2%)	1 (<1%)
		Abdominal pain ^a	139 (12%)	15 (1%)	0
	Common	Stomatitis	96 (8%)	4 (<1%)	0
		Dyspepsia	83 (7%)	2 (<1%)	0
		Flatulence	43 (4%)	0	0
		Abdominal distension	36 (3%)	2 (<1%)	0
		Mouth ulceration	28 (2%)	3 (<1%)	0
		Dry mouth	27 (2%)	0	0
		Uncommon	Pancreatitis	8 (<1%)	4 (<1%)
	Rectal haemorrhage		8 (<1%)	2 (<1%)	0
	Haematochezia		6 (<1%)	0	0
	Gastrointestinal haemorrhage		4 (<1%)	2 (<1%)	0
	Melaena		4 (<1%)	1 (<1%)	0
	Frequent bowel movements		3 (<1%)	0	0
	Anal haemorrhage		2 (<1%)	0	0
	Large intestine perforation		2 (<1%)	1 (<1%)	0
	Mouth haemorrhage		2 (<1%)	0	0
	Upper gastrointestinal haemorrhage		2 (<1%)	1 (<1%)	0
	Enterocutaneous fistula		1 (<1%)	0	0
	Haematemesis		1 (<1%)	0	0
	Haemorrhoidal haemorrhage		1 (<1%)	0	0
	Ileal perforation		1 (<1%)	0	1 (<1%)
	Oesophageal haemorrhage		1 (<1%)	0	0
	Retroperitoneal haemorrhage		1 (<1%)	0	0
	Hepatobiliary disorders	Common	Hyperbilirubinaemia	38 (3%)	2 (<1%)
Hepatic function abnormal			29 (3%)	13 (1%)	2 (<1%)
Hepatotoxicity			18 (2%)	11 (<1%)	2 (<1%)
Uncommon		Jaundice	3 (<1%)	1 (<1%)	0
		Drug induced liver injury	2 (<1%)	2 (<1%)	0
		Hepatic failure	1 (<1%)	0	1 (<1%)
Skin and	Very common	Hair colour change†	404 (35%)	1 (<1%)	0

subcutaneous disorders		Palmar-plantar erythrodysesthesia syndrome	206 (18%)	39 (3%)	0	
		Alopecia	130 (11%)	0	0	
		Rash	129 (11%)	7 (<1%)	0	
	Common		Skin hypopigmentation	52 (5%)	0	0
			Dry skin	50 (4%)	0	0
			Pruritus	29 (3%)	0	0
			Erythema	25 (2%)	0	0
			Skin depigmentation	20 (2%)	0	0
			Hyperhidrosis	17 (1%)	0	0
		Uncommon		Nail disorders	11 (<1%)	0
			Skin exfoliation	10 (<1%)	0	0
			Photosensitivity reaction	7 (<1%)	0	0
			Rash erythematous	6 (<1%)	0	0
			Skin disorder	5 (<1%)	0	0
			Rash macular	4 (<1%)	0	0
			Rash pruritic	3 (<1%)	0	0
			Rash vesicular	3 (<1%)	0	0
	Pruritus generalised		2 (<1%)	1 (<1%)	0	
	Rash generalised		2 (<1%)	0	0	
	Rash papular		2 (<1%)	0	0	
	Plantar erythema		1 (<1%)	0	0	
Musculoskeletal and connective tissue disorders	Common		Arthralgia	48 (4%)	8 (<1%)	0
		Myalgia	35 (3%)	2 (<1%)	0	
		Muscle spasms	25 (2%)	0	0	
	Uncommon	Musculoskeletal pain	9 (<1%)	1 (<1%)	0	
Renal and urinary disorders	Very Common	Proteinuria	135 (12%)	32 (3%)	0	
	Uncommon	Haemorrhage urinary tract	1 (<1%)	0	0	
Reproductive system and breast disorders	Uncommon	Menorrhagia	3 (<1%)	0	0	
		Vaginal haemorrhage	3 (<1%)	0	0	
		Metrorrhagia	1 (<1%)	0	0	
General disorders and administration site conditions	Very common	Fatigue	415 (36%)	65 (6%)	1 (<1%)	
	Common	Mucosal inflammation	86 (7%)	5 (<1%)	0	
		Asthenia	82 (7%)	20 (2%)	1 (<1%)	
		Oedema ^b	72 (6%)	1 (<1%)	0	
		Chest pain	18 (2%)	2 (<1%)	0	
	Uncommon	Chills	4 (<1%)	0	0	
		Mucous membrane disorder	1 (<1%)	0	0	
Investigations	Very common	Alanine aminotransferase increased	246 (21%)	84 (7%)	14 (1%)	
		Aspartate aminotransferase increased	211 (18%)	51 (4%)	10 (<1%)	
	Common	Weight decreased	96 (8%)	7 (<1%)	0	
		Blood bilirubin increased	61 (5%)	6 (<1%)	1 (<1%)	
		Blood creatinine increased	55 (5%)	3 (<1%)	0	

		Lipase increased	51 (4%)	21 (2%)	7 (<1%)
		White blood cell count decreased ^d	51 (4%)	3 (<1%)	0
		Blood thyroid stimulating hormone increased	36 (3%)	0	0
		Amylase increased	35 (3%)	7 (<1%)	0
		Gamma-glutamyltransferase increased	31 (3%)	9 (<1%)	4 (<1%)
		Blood pressure increased	15 (1%)	2 (<1%)	0
		Blood urea increased	12 (1%)	1 (<1%)	0
		Liver function test abnormal	12 (1%)	6 (<1%)	1 (<1%)
	Uncommon	Hepatic enzyme increased	11 (<1%)	4 (<1%)	3 (<1%)
		Blood glucose decreased	7 (<1%)	0	1 (<1%)
		Electrocardiogram QT prolonged	7 (<1%)	2 (<1%)	0
		Transaminase increased	7 (<1%)	1 (<1%)	0
		Thyroid function test abnormal	3 (<1%)	0	0
		Blood pressure diastolic increased	2 (<1%)	0	0
		Blood pressure systolic increased	1 (<1%)	0	0

†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:

^a Abdominal pain, abdominal pain upper and abdominal pain lower

^b Oedema, oedema peripheral, eye oedema, localised oedema and face oedema

^c Dysgeusia, ageusia and hypogeusia

^d White cell count decreased, neutrophil count decreased and leukocyte count decreased

^e Decreased appetite and anorexia

^f Cardiac dysfunction, left ventricular dysfunction, cardiac failure and restrictive cardiomyopathy

^g Venous thromboembolic event, deep vein thrombosis, pulmonary embolism and thrombosis

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

בברכה,
יעל לוי טל
רוקחת ממונה
נוברטיס ישראל