

PART III: CONSUMER INFORMATION

VOTRIENT®
Pazopanib Tablets

This leaflet is part III of a three-part "Product Monograph" published when VOTRIENT® was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about VOTRIENT. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

VOTRIENT is used in the treatment of:

Metastatic kidney cancer (when cancer cells have spread from the kidney to other parts of the body).

Selective subtypes of advanced soft tissue sarcoma in patients who have received prior chemotherapy. Soft tissue sarcoma is a type of cancer that occurs in muscles, blood vessels or other tissues that support, surround and protect the organs.

VOTRIENT is shown to slow tumour growth, however, it is not known whether VOTRIENT prolongs overall survival or improves the quality of life of patients.

What it does:

VOTRIENT prevents the activity of a special group of proteins which are known to be involved in the growth and spread of cancer cells.

When it should not be used:

VOTRIENT must not be used if you are allergic to pazopanib hydrochloride, or any of the other ingredients in VOTRIENT (see **What the important nonmedicinal ingredients are**).

VOTRIENT must not be used in children under two years of age.

What the medicinal ingredient is:

The active ingredient is pazopanib hydrochloride.

What the important nonmedicinal ingredients are:

The other ingredients are hypromellose, macrogol 400,

magnesium stearate, microcrystalline cellulose, povidone (K30), polysorbate 80, sodium starch glycolate, titanium dioxide (E171), iron oxide black (E172) and iron oxide yellow (E172).

What dosage forms it comes in:

VOTRIENT® is available as tablets. Each film coated tablet contains either 200 mg or *400 mg of pazopanib hydrochloride. The 200 mg tablets of VOTRIENT are modified capsule shaped, grey, film coated with GS JT debossed on one side and are available in bottles of 120 tablets.

The *400 mg tablets are modified capsule shaped, yellow, film coated with GS UHL debossed on one side and are available in bottles of 30 tablets or 60 tablets.

*VOTRIENT 400 mg tablets not available in Canada

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

VOTRIENT should be prescribed and managed by a doctor experienced in the use of cancer drugs.

VOTRIENT is not recommended for patients with moderate or severe liver impairment (reduced function).

Serious side effects with the use of VOTRIENT may include the following:

- Liver toxicity
- High blood pressure
- Effect on the electrical activity of the heart (QT/QTc prolongation)
- Heart becomes less effective at pumping blood (cardiac dysfunction)
- Blood clots (arterial thromboembolic or venous thrombotic events and thrombotic microangiopathy)
- Bleeding
- Gastrointestinal perforation (a hole that develops through the wall of the stomach, small intestine or large bowel) and fistula (an abnormal connection between parts of the digestive tract)
- Reversible swelling in the rear part of the brain that can be associated with high blood pressure and can lead to headache, loss of speech or vision, abnormal drowsiness, confusion and/or seizure (Posterior Reversible Encephalopathy Syndrome or Reversible Posterior Leukoencephalopathy Syndrome)

Safety and efficacy of VOTRIENT have not been established in children less than 18 years of age. VOTRIENT must not be used in children under two years of age.

BEFORE you use VOTRIENT talk to your doctor or pharmacist:

- If you have or had heart disease, heart failure or heart attack
- If you have or have had a heart rhythm disorder such as irregular heartbeat, prolongation of the QT interval or any risk factors for Torsade de Pointes (dangerous rapid fluttering of the heart) such as diabetes, low potassium, magnesium or calcium levels, or a history of low heart rate, fainting, or loss of consciousness
- If you have high blood pressure
- If you have liver disease
- If you have problems with bleeding
- If you have gastrointestinal problems
- If you have or had a blood clot in a vein or in a lung
- If you have had prior collapse of a lung
- If you have a kidney problem
- If you have thyroid problems
- If you are going to have a surgical or dental procedure, or if you have had either recently

While you are taking VOTRIENT your doctor will take blood samples to check for any liver problems. You should report any signs or symptoms of liver injury including jaundice (yellowing of whites of eyes or skin), unusual darkening of the urine, anorexia (loss of appetite), nausea, fatigue, right upper abdominal discomfort and vomiting. Your doctor will also take urine samples to check for any kidney problems. You will also have your blood pressure checked. Your doctor will periodically record your electrocardiogram (ECG) to check your heart's electrical conduction.

Your doctor will also check on any recent surgical or dental procedures to see if you are healing properly.

Use a reliable method of contraception to avoid becoming pregnant while you're taking VOTRIENT and for up to 8 weeks after you stop treatment with VOTRIENT. If you are pregnant or think you could be, talk to your doctor about the risks and benefits to you and your baby while taking VOTRIENT. Your doctor may recommend that you don't take VOTRIENT while you are pregnant.

Male patients (including those who have had vasectomies) with sexual partners who are pregnant, possibly pregnant, or

who could become pregnant should use condoms during sexual intercourse while taking VOTRIENT and for at least 2 weeks after the last dose of drug.

Breastfeeding is not recommended during treatment with VOTRIENT. Ask your doctor for advice.

INTERACTIONS WITH THIS MEDICATION

Tell your doctor or pharmacist if you are taking, or have recently taken any other medicines including any medicines you bought without a prescription. This includes herbal medicines.

Some medicines may affect the way VOTRIENT works or VOTRIENT may affect how other medicines work. These include:

- clarithromycin, ketoconazole, itraconazole, telithromycin, voriconazole (used to treat infections)
- atazanavir, indinavir, nelfinavir, ritonavir, saquinavir (used to treat HIV)
- dextromethorphan (used in cough medicines)
- simvastatin and possibly other statins (used to treat high cholesterol levels)
- medicines that reduce stomach acid (e.g. esomeprazole, ranitidine, magnesium hydroxide)

Also, the following list includes some, but not all, of the drugs that may interact with VOTRIENT to affect the electrical activity of your heart:

- Antiarrhythmics (drugs that stabilize the heart rhythm function, such as quinidine, procainamide, amiodarone, sotalol, etc.)
- Antidepressants (mood disorder drugs)
- Antipsychotics (drugs used to stabilize thinking and behaviour)
- Opioids (e.g. methadone)
- Macrolide antibiotics (such as erythromycin, clarithromycin)
- Fluoroquinolone antibiotics (such as moxifloxacin, levofloxacin, ciprofloxacin)
- Antifungals (such as fluconazole, voriconazole)
- Antimalarials (e.g. quinine)
- Antinauseants (e.g. granisetron, ondansetron, dolasetron)
- Anti-asthmatics (e.g. salmeterol, formoterol)
- Tacrolimus (used after organ transplant to prevent rejection)
- Certain anticancer treatments (e.g. sunitinib, nilotinib, lapatinib, sorafenib, vorinostat)

VOTRIENT is affected by food intake (see PROPER USE OF THIS MEDICATION). You should not drink grapefruit juice or eat grapefruit while you are being treated with VOTRIENT as this may increase the chance of side effects.

PROPER USE OF THIS MEDICATION

Always take VOTRIENT exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Usual dose:

The usual dose is 800 mg VOTRIENT, taken once a day.

Do not take more than 800 mg VOTRIENT a day.

Swallow the tablets whole with water, one after the other, at about the same time each day. Do not break or crush the tablets as it affects the way the medicine is absorbed and may increase the chance of side effects.

It is important that you take VOTRIENT either at least one hour before or at least two hours after food.

Depending on your response to treatment, your doctor may recommend adjusting your dose or temporarily stopping your treatment.

Overdose:

If you have accidentally taken more VOTRIENT tablets than you should, contact your doctor, or poison control centre, or go to the emergency room of the nearest hospital even if there are no symptoms.

Missed Dose:

If you forget to take VOTRIENT, do not take a double dose to make up for a missed dose. Take the next dose at the scheduled time.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all medicines, VOTRIENT can cause side effects.

Very common side effects - these may affect more than 1 in 10 people:

- diarrhea (which can be severe; e.g. with fever or 3 or more times a day)
- feeling or being sick (nausea or vomiting)

- loss of appetite
- stomach pain or discomfort
- high blood pressure
- headache
- loss of strength
- lack of energy
- weakness
- changes in hair colour
- weight loss
- problems with taste
- skin rash
- a skin reaction or pain on the palms of the hands or soles of the feet (including tingling, numbness, pain, swelling or reddening)
- dizziness
- cough
- shortness of breath
- chest pain
- swelling of hands, ankles or feet
- muscle pain
- pain in the bones, muscles, ligaments, joints and tendons
- mouth sores
- unusual hair loss or thinning
- loss of skin pigment
- slow heart rate
- tumour pain
- increase in some substances (enzymes) produced by the liver

Common side effects - these may affect up to 1 in 10 people:

- temporary reduction in blood supply to the brain (mini-stroke)
- reduction of blood supply to the heart (angina)
- changes in the heart's electrical conduction (QT-prolongation) which may cause irregular heartbeat
- heart attack
- severe bleeding in the lung
- under-active thyroid gland
- abnormal liver function (which can be severe and may cause yellowing of the skin or the whites of the eyes (jaundice), unusual darkening of the urine, unusual tiredness, or right upper stomach area pain)
- indigestion
- flatulence
- nosebleeds
- dry skin
- nail disorder
- hoarseness
- blurred vision
- chills
- urinary tract infection
- blood in the urine

- painful urination
- sudden collapse of a lung
- heart becomes less effective at pumping blood (cardiac dysfunction)
- excessive sweating
- atypical prickling or crawling sensations on the skin
- sore mouth or mouth ulcers
- blood clot in your body (you might feel chest pain, shortness of breath, leg pain, and swelling of the legs/feet). Such blood clots can break off and travel to your lungs which may be life-threatening or even fatal
- muscle spasms
- difficulty sleeping
- severe bleeding from the esophagus, stomach, intestine or anus. Symptoms can include vomiting blood, passing blood with or in the stools or black stools
- a decrease in the number of cells involved in blood clotting (thrombocytopenia)
- low white blood cell count (neutropenia, leucopenia, lymphopenia)
- protein in urine
- increase in bilirubin (a substance produced by the liver)
- decrease in albumin (a protein found in the blood)
- increase in lipase (an enzyme from the pancreas)
- increased potassium in the blood
- infections, with or without changes in white blood cells (cells that fight infection).
- blood clots accompanied by a decrease in red blood cells and cells involved in clotting (thrombotic microangiopathy [TMA] including thrombotic thrombocytopenic purpura [TTP] and hemolytic uremic syndrome [HUS]). These clots may harm organs such as the brain and kidneys. Symptoms may include fatigue, abdominal pain, fever, confusion, bruising under the skin, or bleeding of the nose or gums. You may also get less urine or blood in the urine.

Side Effects with Unknown Frequency:

- Interstitial lung disease, a form of lung scarring or inflammation, can have a fatal outcome in some cases. If you develop symptoms such as sudden difficulty of breathing associated with cough or fever contact your doctor immediately.
- reversible swelling in the rear part of the brain that can be associated with high blood pressure and can lead to headache, loss of speech or vision, abnormal drowsiness, confusion and/or seizure (Posterior Reversible Encephalopathy Syndrome or Reversible Posterior Leukoencephalopathy Syndrome)

If you get side effects tell your doctor or pharmacist if any of the side effects listed becomes severe or troublesome, or if you notice any side effects not listed in this leaflet.

Uncommon side effects - these may affect up to 1 in 100 people:

- stroke
- severe bleeding (haemorrhage) in brain
- a dangerous rapid fluttering of the heart (Torsade de Pointes)
- hole (perforation) in digestive tract
- abnormal connection between parts of the digestive tract (fistula)
- a sudden and severe rise in blood pressure which may be life-threatening
- liver failure
- Inflammation of the pancreas
- Separation or tear of the lining of the back part of the eye (retinal detachment or tear). This can result in trouble seeing (blurry or impaired vision).
- Abnormal increase in concentration of hemoglobin in the blood

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect	Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
	Only if severe	In all cases	
Very common			
chest pain		✓	
Common			
diarrhea		✓	
symptoms of abnormal liver function (see above); -if yellowing of the skin or eyes appears		✓	✓
increased blood pressure		✓	
temporary reduction in blood supply to the brain (mini-stroke)		✓	
reduction of blood supply to the heart (angina)		✓	
blood clots causing chest pain, shortness of breath, leg pain, swelling of the legs/feet		✓	
decreased amount of blood pumped out of the heart with symptoms such as shortness of breath, fatigue, swollen feet and ankles		✓	
severe bleeding from the esophagus, stomach, intestine or anus. Symptoms can include vomiting blood, passing blood with or in the stools or black stools.			✓

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect	Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
	Only if severe	In all cases	
Uncommon			
severe bleeding in lung			✓
heart problems, which may cause irregular heartbeat; -with symptoms of dizziness or palpitations		✓	✓
-if you experience seizures, fainting or loss of consciousness			✓
stroke			✓
Blood clots accompanied by a decrease in red blood cells and cells involved in clotting (thrombotic microangiopathy [TMA] including thrombotic thrombocytopenic purpura [TTP] and hemolytic uremic syndrome [HUS]). Symptoms may include fatigue, abdominal pain, fever, confusion, bruising under the skin, or bleeding of the nose or gums. You may also get less urine or blood in the urine			✓
Rare			
Blurry or impaired vision		✓	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect	Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
	Only if severe	In all cases	
Unknown Frequency			
Cough, shortness of breath, fever (interstitial lung disease)		✓	
Headaches, seizures, loss of speech or vision, high blood pressure, abnormal drowsiness			✓

This is not a complete list of side effects. For any unexpected effects while taking VOTRIENT, contact your doctor or pharmacist.

HOW TO STORE IT

Keep out of the reach and sight of children. Do not use VOTRIENT after the expiry date.

Store between 15°C - 30°C.

If you have any unwanted tablets do not put them in waste water or household rubbish. Ask your pharmacist how to dispose of tablets you do not need. This will help to protect the environment.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
 - Fax toll-free to 1-866-678-6789, or
 - Mail to: Canada Vigilance Program
Health Canada
Postal Locator 0701E
Ottawa, ON K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of the side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at:

<http://www.novartis.ca> or by contacting the sponsor,

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