PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrVOTRIENT®

Pazopanib tablets

Read this carefully before you start taking **VOTRIENT®** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **VOTRIENT**.

Serious Warnings and Precautions

Only take VOTRIENT under the care of a doctor who knows how to use anti-cancer drugs.

VOTRIENT is not recommended for patients with moderate or severe liver problems (reduced function). Your healthcare professional will monitor your liver function during treatment with VOTRIENT.

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

- **Liver toxicity**
- **High blood pressure**
- **QT/QTc prolongation** (Changes in the electrical activity of the heart)
- **Heart problems** (Heart becomes less effective at pumping blood)
- **Blood clots** in arteries (**arterial thromboembolic events**), in veins (**venous thrombotic events**) or small blood vessels (**thrombotic microangiopathy**)
- **Bleeding problems**
- **Gastrointestinal perforation** (a hole that develops in the wall of the stomach or intestines) and **fistula** (an abnormal connection between parts of the digestive tract)
- **Posterior Reversible Encephalopathy Syndrome or Reversible Posterior Leukoencephalopathy Syndrome** (Reversible swelling in the back of the brain)
- **Tumor Lysis syndrome** (a complication due to the breakdown of cancer cells)
  This is a serious condition that can happen with the sudden death of cancer cells. Your healthcare professional will monitor you for signs of Tumour Lysis Syndrome.

What is VOTRIENT used for?

VOTRIENT is used to treat adults with:

- 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 NOT recommended for use in children and adolescents under 18 years of age.

How does VOTRIENT work?

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

What are the ingredients in VOTRIENT?

Medicinal ingredient: pazopanib hydrochloride

Non-medicinal ingredients: hypromellose, iron oxide black (E172) or iron oxide red (E172), macrogol 400, magnesium stearate, microcrystalline cellulose, polysorbate 80, povidone (K30), sodium starch glycollate and titanium dioxide (E171).

VOTRIENT comes in the following dosage forms:

Film coated tablets: 200 mg

Do not use VOTRIENT if:

- you are allergic to pazopanib hydrochloride, or any of the other ingredients in VOTRIENT.

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

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take VOTRIENT. Talk about any health conditions or problems you may have, including if you:

- have or had heart disease, heart failure or heart attack
- have or have had a heart rhythm disorder such as: irregular heartbeat, prolongation of the QT interval
- have or have had 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
- have problems with your blood pressure and its complications, including enlargement and weakening of a blood vessel (aneurysm) and separation of the layers of the arterial wall (Artery Dissection)
- have liver disease
- have bleeding problems
- have gastrointestinal problems
- have or had a blood clot in a vein or in a lung
- have had prior collapse of a lung
- have a kidney problem
- have thyroid problems
- recently have had or are planning to have a surgery or dental procedure

Other warnings you should know about:

Monitoring and laboratory testing:

While you are taking VOTRIENT your doctor will take blood samples to check for any liver problems. 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.

Fertility:

VOTRIENT may decrease your ability to have children. Talk to your healthcare professional if this is a concern for you.

Pregnancy, birth control and breastfeeding:

Female patients

- Avoid becoming pregnant while taking VOTRIENT. It may harm your unborn baby.
- Use a reliable method of birth control to avoid becoming pregnant while you're taking VOTRIENT and for up to 8 weeks after you stop treatment with VOTRIENT.
- Tell your healthcare professional right away if you become or think you are pregnant while taking VOTRIENT.
- It is not known if VOTIRENT passes into breast milk. Do NOT breastfeed while you are taking VOTRIENT. Talk to your healthcare professional about the best way to feed your baby during treatment.

Male patients

- During treatment with VOTRIENT, use condoms each time you have sex with women who are pregnant, possibly pregnant, or who could become pregnant. Continue using condoms for at least 2 weeks after your last dose of VOTRIENT.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with VOTRIENT:

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

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

- antiarrhythmics (medicines that stabilize the heart rhythm function, e.g. quinidine, procainamide, amiodarone, sotalol)
- antidepressants (mood disorder medicines, e.g. amitriptyline, imipramine, maproptiline, fluoxetine, citalopram, venlafaxine)
- antipsychotics (medicines used to stabilize thinking and behaviour, e.g. chlorpromazine, pimozide, haloperidol, droperidol, ziprasidone)

- opioids (e.g. methadone)
- medicines used to treat bacterial infections such as:
    - macrolide antibiotics (e.g. erythromycin, clarithromycin, telithromycin)
    - fluoroquinolone antibiotics (e.g. moxifloxacin, levofloxacin, ciprofloxacin)
- medicines used to treat fungal infections (e.g. fluconazole, voriconazole)
- medicines used to treat malaria (e.g. quinine)
- medicines for nausea (e.g. granisetron, ondansetron, dolasetron)
- medicines used to treat asthma (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. 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.

How to take VOTRIENT:

- Always take VOTRIENT exactly as your healthcare professional tells you. Check with your doctor, nurse or pharmacist if you are not sure.
- Do NOT take with food. It is important that you take VOTRIENT either at least one hour before or at least two hours after food.
- 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.

Usual dose:

The usual dose is 800 mg (four 200 mg tablets), taken once a day.

Do NOT take more than 800 mg VOTRIENT a day.

Depending on your response to treatment, your doctor may adjust your dose or temporarily stop your treatment.

Overdose:

If you think you, or a person you are caring for, have taken too much VOTRIENT, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you forget to take VOTRIENT, and your next dose is in:

- Less than 12 hours, skip the missed dose. Take your next dose at the regular time.
- 12 hours or more, take the missed dose as soon as you remember. The next dose can be taken at the regular time.

Do NOT take a double dose to make up for a missed dose.

What are possible side effects from using VOTRIENT?

These are not all the possible side effects you may have when taking VOTRIENT. If you experience any side effects not listed here, tell your healthcare professional.

Side effects may include:

- feeling or being sick (nausea or vomiting)
- loss of appetite
- stomach pain or discomfort
- weight loss
- problems with taste
- sore mouth, mouth ulcers or sores
- indigestion
- flatulence
- headache
- loss of strength
- lack of energy
- weakness
- difficulty sleeping
- dizziness
- changes in hair colour
- skin rash
- unusual hair loss or thinning
- loss of skin pigment
- dry skin
- nail disorder
- unusual prickling or crawling sensations on the skin
- excessive sweating
- hoarseness
- nosebleeds
- cough
- shortness of breath
- swelling of hands, ankles or feet
- muscle pain
- muscle spasms
- pain in the bones, muscles, ligaments, joints and tendons
- slow heart rate
- tumour pain
- increase in some substances (enzymes) produced by the liver (shown in blood tests)
- under-active thyroid gland (shown in blood tests)
- chills
- urinary tract infection
- blood in the urine
- painful urination
- infections, with or without changes in white blood cells (cells that fight infection)

VOTRIENT can cause abnormal blood and urine test results. Your doctor will decide when to perform

blood and urine tests and will interpret the results.

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.

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
VERY COMMON			
Palmar-plantar erythrodysaesthesia syndrome (skin reaction also known as hand-foot syndrome): pain, tingling, swelling or redness, thick calluses and blisters on the palms of the hands or soles of the feet	✓		
Chest pain		✓	
COMMON			
QT-prolongation (changes in the heart's electrical conduction): irregular heartbeat, fainting, loss of consciousness, seizures		✓	
Myocardial infarction (heart attack, the supply of blood to the heart is suddenly blocked): pressure, tightness, pain, or a squeezing or aching sensation in chest or arms			✓
Pneumothorax (sudden collapse of a lung): sudden chest pain and shortness of breath			✓
Diarrhea: severe, 3 or more loose or liquid bowel movements in a day; may be accompanied by fever		✓	
Liver problems and/or liver failure: yellowing of the skin and eyeballs (jaundice), dark urine, pain in your right abdomen, abdominal swelling, nausea, vomiting, a general sense of feeling unwell (malaise), disorientation or confusion or sleepiness			✓
Hypertension (increased blood pressure): can be sudden and severe, may be life-threatening;		✓	

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
headache, stronger and possibly faster heartbeat			
Transient ischemic attack (mini-stroke, temporary reduction in blood supply to the brain): numbness or weakness on one side of the body, difficulty speaking, dizziness, loss of balance. Symptoms can last from a few minutes to several hours.		✓	
Angina (reduction of blood supply to the heart): discomfort in the shoulder, arm, back, throat, jaw or teeth; pain or pressure in the chest		✓	
Deep vein thrombosis or pulmonary embolism (blood clots in the veins of the arms, legs or lungs): chest pain, shortness of breath, leg pain, swelling of the legs/feet		✓	
Heart failure (decreased amount of blood pumped out of the heart): shortness of breath, fatigue, swollen feet and ankles		✓	
Hemorrhage (severe bleeding from the esophagus, stomach, intestine or anus): vomiting blood, passing blood with or in the stools or black stools			✓
UNCOMMON			
Pulmonary haemorrhage (severe bleeding in lung): coughing up blood			✓
Cerebral haemorrhage (severe bleeding in brain): a sudden severe headache, seizures, weakness in an arm or leg, lethargy, changes in vision, difficulty speaking or understanding speech, loss of coordination, loss of balance, loss of consciousness			✓
Torsade de Pointes (a dangerous rapid fluttering of the heart): heart			✓

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
palpitations, dizziness, nausea, cold sweats, chest pain, shortness of breath, rapid pulse or low blood pressure			
Heart problems including irregular heartbeat: dizziness, palpitations, cold sweats, chest pain, shortness of breath, rapid pulse or low blood pressure		✓	
Stroke (poor blood flow to the brain): sudden numbness or weakness of your arm, leg or face, especially if only on one side of the body; difficulty speaking sudden difficulty in walking or loss of balance or coordination			✓
Thrombotic microangiopathy [TMA], including thrombotic thrombocytopenic purpura [TTP] and hemolytic uremic syndrome [HUS] (blood clots accompanied by a decrease in red blood cells and cells involved in clotting): bruising under the skin, bleeding of the nose or gums, less urine, blood in the urine			✓
Gastrointestinal perforation (hole in digestive tract): abdominal pain or tenderness, bloating or a feeling of fullness (distention) in abdomen			✓
Fistula (abnormal connection between parts of the digestive tract): diarrhea, rectal bleeding, weight loss, dehydration			✓
Pancreatitis (inflammation of the pancreas): abdominal pain that lasts and gets worse when you lie down, nausea, vomiting			✓
Retinal detachment or tear (separation or tear of the lining of the back part of the eye): trouble seeing, blurry or impaired vision			✓

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Skin Ulcer (skin wound with no healing tendency)			✓
RARE			
Artery dissection (sudden severe pain in the back, chest or abdomen)			✓
Artery aneurysm (a bulge in the wall of any artery including in the chest, arms, legs, heart, and brain): symptoms will differ by the site. They can be cough, coughing up blood, strong pain high in your neck or in your back when you didn't hurt yourself, problems swallowing, hoarse voice, unusual pulsing in your chest or abdomen			✓
UNKNOWN FREQUENCY			
Interstitial lung disease (a form of lung scarring or inflammation, can have a fatal outcome in some cases): cough, shortness of breath, difficulty breathing, fever		✓	
Posterior Reversible Encephalopathy Syndrome or Reversible Posterior Leukoencephalopathy Syndrome (reversible swelling in the rear part of the brain): headaches, seizures, loss of speech or vision, high blood pressure, abnormal drowsiness, confusion, seizure			✓
Tumour lysis syndrome (the sudden, rapid death of cancer cells due to the treatment): nausea, shortness of breath, irregular heartbeat, heart rhythm disturbances, lack of urination, clouding of urine, muscle spasms or twitching, tiredness and/or joint pain, severe muscle weakness, and seizures. Metabolic disorders (kidney failure, abnormal heartbeat) and abnormal blood			✓

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
tests due to rapid breakdown of cancer cells.			

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store between 15°C to 30°C.

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

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

If you want more information about VOTRIENT:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; the manufacturer's website www.novartis.ca, or by calling 1-800-363-8883.

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