

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

Pr**CABOMETYX**[®] **cabozantinib tablets**

Read this carefully before you start taking **CABOMETYX** 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 **CABOMETYX**.

Your cancer will be treated with **CABOMETYX**. You may also receive another medication called nivolumab. If this applies to you, read the Patient Medication Information leaflet for nivolumab as well as this one.

Serious Warnings and Precautions

CABOMETYX should only be prescribed and used under the supervision of a healthcare professional experienced in drugs to treat cancer.

Serious side-effects with **CABOMETYX** can include:

- Life-threatening blood clots
- High blood pressure. Blood pressure can be severely high and could cause stroke (hypertensive crisis).
- Life-threatening tear in your stomach or intestinal wall (**perforation**) or abnormal connection between 2 parts of your body (**fistula**)
- Life-threatening bleeding
- Life-threatening liver injury
- A condition called **posterior reversible leukoencephalopathy syndrome**
- Abnormal wound healing

CABOMETYX has not been studied in patients with heart problems or severe kidney or liver problems.

What is **CABOMETYX used for?**

CABOMETYX is used to treat adults with:

- a type of advanced kidney cancer called renal cell carcinoma. These patients may or may not have received prior treatments.
 - **CABOMETYX** may also be given with another medicine called nivolumab. This is given to patients who have not received any previous treatments for their disease. These patients:
 - cannot be treated with radiation or surgery
 - have a cancer that has spread to other parts of the body
- a type of liver cancer called hepatocellular carcinoma. These patients will have been previously treated with a medication called sorafenib.
- a type of thyroid cancer called differentiated thyroid carcinoma. **CABOMETYX** is used when the cancer has spread to nearby tissues or to other parts of the body. These

patients will:

- have been previously treated with anticancer medications and;
- no longer respond to the radioactive iodine treatment. Or are not able to receive radioactive iodine treatment.

How does CABOMETYX work?

CABOMETYX is a multi-kinase inhibitor. It works by blocking the action of proteins called receptor tyrosine kinases (RTKs). RTKs are involved in cell growth and the development of new blood vessels. These proteins can be present in high amounts in cancer cells. By blocking their action, CABOMETYX can slow down how fast the tumour grows, help to block the blood supply that the cancer needs and may increase the length of time before the cancer gets worse.

What are the ingredients in CABOMETYX?

Medicinal ingredient: cabozantinib (S)-malate

Non-medicinal ingredients: colloidal silicon dioxide, croscarmellose sodium, hydroxypropyl cellulose, hypromellose 2910, iron oxide yellow, lactose anhydrous, magnesium stearate, microcrystalline cellulose, titanium dioxide and triacetin

CABOMETYX comes in the following dosage forms:

Tablets: 20 mg, 40 mg, 60 mg cabozantinib (as cabozantinib (S)-malate)

Do not use CABOMETYX if:

You are allergic to cabozantinib or any other ingredients in this medicine including lactose anhydrous.

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

- have high blood pressure and its complications, including separation of the layers of an artery wall (artery dissection)
- have heart disease
- have diarrhea
- have any unusual bleeding or a history of bleeding. This includes blood in stool, vomiting or coughing up blood.
- plan to have any surgery, including dental surgery. You should stop treatment with CABOMETYX at least 28 days before any scheduled surgery.
- have liver or kidney disease, including increased amounts of protein in your urine
- have inflammatory bowel disease (for example Crohn's disease or ulcerative colitis, diverticulitis, or appendicitis)
- have had a blood clot in the leg, lungs or liver, stroke, or heart attack
- have any heart disorder, including an irregular heartbeat, prolongation of the QT interval or a family history of QT prolongation or sudden cardiac death at less than 50 years of age
- have thyroid problems
- are pregnant, or plan to become pregnant. Avoid getting pregnant while taking CABOMETYX, as it can harm your unborn baby.
 - Female patients who are able to become pregnant, should use effective

methods of birth control during treatment and for 4 months after your last dose of CABOMETYX.

- Talk to your healthcare provider about birth control methods that may be right for you.
- If you become pregnant or think you are pregnant, tell your healthcare provider right away.
- are a male patient with a female partner who is able to become pregnant. Your female partner should avoid getting pregnant while you are taking CABOMETYX.
 - Effective birth control should be used during treatment with CABOMETYX and for 4 months after your last dose.
 - Tell your healthcare professional right away if your partner becomes pregnant while you are receiving treatment with CABOMETYX.
- are breastfeeding or plan to breastfeed. It is not known if CABOMETYX passes into your breast milk. Do not breastfeed during treatment and for 4 months after your last dose of CABOMETYX.

Other warnings you should know about:

- CABOMETYX in combination with nivolumab can cause **adrenal insufficiency**. This condition happens when the adrenal glands don't make enough of the hormone cortisol. If you experience adrenal insufficiency, you may need to take other medications.
- **Check-ups and testing:** You will have regular visits with a healthcare professional before and during your treatment with CABOMETYX. At these visits, your healthcare professional may:
 - check your heart rate and blood pressure. You may also need an electrocardiogram.
 - check your mouth and jaw.
 - do blood tests. The results of these test will tell your healthcare professional how CABOMETYX is affecting your blood, thyroid and liver.

Driving and using machines: Before you do tasks which may require special attention, wait until you know how you respond to CABOMETYX. If you feel dizzy, weak, or tired, do not drive or use tools or machines.

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 CABOMETYX:

- Medicines that treat fungal infections, such as itraconazole, ketoconazole, and posaconazole
- Medicines used to treat bacterial infections (antibiotics) such as erythromycin, clarithromycin, and rifampicin
- Allergy medicines such as fexofenadine
- Medicines used to treat epilepsy or fits such as phenytoin, carbamazepine, and phenobarbital
- Herbal preparations containing St. John's Wort (*Hypericum perforatum*), sometimes used for treating depression or depression-related conditions such as anxiety
- Medicines used to thin the blood, such as warfarin, dabigatran, etexilate
- Medicines to treat high blood pressure or other heart conditions, such as ambrisentan,

- aliskeren, talinolol, digoxin, and tolvaptan
- Medicines for diabetes, such as saxagliptin and sitagliptin
- Medicines used to treat gout, such as colchicine
- Medicines used to treat HIV or AIDS, such as efavirenz, ritonavir, maraviroc and emtricitabine
- Medicines used to lower high cholesterol in the blood or to remove substances called bile acids from your body, such as cholestyramin and cholestagel
- Medicines that may lengthen the QT-interval of your heart, such as certain drugs to treat heart conditions, psychosis, depression, pain, infections and other conditions
- Medicines that may affect the levels of electrolytes in your body, such as certain diuretics, laxatives, enemas and corticosteroids

How to take CABOMETYX:

- Always take CABOMETYX exactly as your healthcare professional tells you to take it.
- Take CABOMETYX once daily on an empty stomach. Do not eat for at least 2 hours before and at least 1 hour after taking the dose.
- Swallow tablets whole with a full glass (at least 8 ounces) of water.
- **Do not** crush tablets.
- Take your medicine at about the same time each day.
- Do not drink grapefruit juice or eat grapefruit while taking CABOMETYX. Do not take supplements that contain grapefruit while taking CABOMETYX.
- Do not stop taking your CABOMETYX without first talking to your healthcare professional.
- If you are taking CABOMETYX with nivolumab:
 - A healthcare professional will give you nivolumab every 2 weeks or every 4 weeks. It is likely to be given to you during the day.
 - Take your CABOMETYX on an empty stomach, preferably in the evening.

Usual dose:

Your healthcare professional will decide on the right dose of CABOMETYX for you to take.

- When CABOMETYX is taken alone, the usual adult dose is 60 mg, once a day.
- When CABOMETYX is taken with nivolumab, the usual adult dose is 40 mg once a day.

Your doctor may adjust your dose, stop treatment for some time (then resume at the same or a different dose) or stop your treatment completely. This may happen if:

- you have surgery,
- you are taking certain other medications,
- you have problems with your liver,
- you have certain side effects while taking CABOMETYX, or
- your disease gets worse.

Overdose:

If you think you, or a person you are caring for, have taken too much CABOMETYX, contact a healthcare professional, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Missed Dose:

If you miss a dose and your next dose is in:

- less than 12 hours, take your next dose at its scheduled time. Do not make up the missed dose.
- 12 hours or more, take the missed dose as soon as you remember. Take your next dose at the normal time.

What are possible side effects from using CABOMETYX?

These are not all the possible side effects you may feel when taking CABOMETYX. If you experience any side effects not listed here, contact your healthcare professional.

- Altered sense of taste
- Cough
- Decreased appetite
- Difficulty in speaking, hoarseness
- Dizziness, fainting
- Dry skin and mouth
- Fatigue, insomnia
- Fever
- Hair loss
- Headache
- Heartburn (bringing up stomach acid)
- Pain in arms, legs and joints, muscle spasms
- Rash or redness and small bruises on the skin, raised purple to red spots on skin (including lumps or open sores)
- Redness, swelling or pain in the mouth or throat
- Ringing in the ears
- Shortness of breath
- Stomach upset, including diarrhea, nausea, vomiting, constipation, indigestion, and abdominal pain
- Swelling in lower legs or hands
- Upper respiratory tract infection
- Weakness
- Weakness or numbness in hands or feet
- Weight loss

CABOMETYX can cause abnormal blood and urine test results. Your healthcare professional will decide when to perform blood or urine tests and will interpret the results.

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			
Hand-foot skin reaction: redness, blisters, pain in the palms of the hands or soles of the feet	X		
Ascites (fluid in the abdomen): abdominal pain, feeling of fullness, flat or pushed out navel, weight increase, shortness of breath		X	

Hypertension (high blood pressure): headaches, vision problems, nausea and vomiting	X		
Anemia (low levels of red blood cells and hemoglobin): fatigue, having pale skin, shortness of breath, loss of energy or weakness	X		
Hypothyroidism (underactive thyroid gland): changes in heart rate, appetite or weight, tiredness, constipation, feeling cold, dry skin, swelling at front of neck		X	
Hyponatremia (low level of sodium in your blood): loss of energy, tiredness, muscle weakness or cramps, seizures	X		
Hypophosphatemia (low level of phosphate in the blood): muscle weakness, coma, bone pain and fractures	X		
Hypomagnesemia (low level of magnesium in the blood): nausea, vomiting, weakness, muscle spasms, tremors	X		
Hypokalemia (low level of potassium in the blood): muscle weakness, cramping	X		
Decreased lymphocytes (low level of white blood cells): swollen lymph nodes, painful swollen joints and rash	X		
Proteinuria (too much protein in your urine): swelling of the hands, feet, face	X		
Hyperthyroidism (high levels of thyroid hormone): anxiety or nervousness, weight loss, frequent and loose bowel movements, breathlessness, feeling hot and possibly feelings of having rapid, fluttering or pounding heart		X	
High levels of liver enzymes (alanine transaminase, aspartate transaminase) or bilirubin in the blood : nausea, vomiting, weight loss, fatigue, yellowing of the skin or eyes, dark urine, itching.		X	
COMMON			
Thromboembolism (blood clot in a vein or artery): pain or tenderness or swelling in your arm or leg, skin that is red or warm, coldness, tingling or numbness, pale skin, muscle pain or spasms, weakness			X
Severe hemorrhage (bleeding): vomiting blood, black stools, bloody urine, headache, coughing up blood			X
Gastrointestinal perforation (tear in your stomach or intestinal wall): abdominal pain, feeling sick, vomiting, constipation, fever			X

Hypocalcemia (low level of calcium in the blood): numbness and tingling in the hands, feet or lips, muscle cramping or spasms, light-headedness, slow heartbeat	X		
Dehydration (condition that happens when you lose more fluid than you take in): thirst, headache, loss of appetite, tiredness, weakness, decreased urine, dark urine	X		
Thrombocytopenia (low level of platelets in the blood): bruising easily, bleeding gums, nosebleeds, more bleeding than expected.	X		
Hepatic encephalopathy (worsening brain function due to liver issues): change in alertness, confusion, mood or personality changes, disorientation, changes in sleep patterns, loss of consciousness, coma		X	
Adrenal insufficiency (when adrenal glands don't make enough cortisol): fatigue, darkening of skin colour, low blood pressure with dizziness or fainting, muscle and joint pain, craving salt.		X	
Hypersensitivity reactions including anaphylaxis and infusion-related reactions (severe allergic reactions): fever, skin rash, hives, itching, swelling, shortness of breath, wheezing, runny nose, difficulty swallowing itchy, watery eyes, feeling sick to your stomach, and throwing up. This side effect is possible when CABOMETYX is taken with nivolumab.		X	
UNCOMMON			
Convulsion: Fits (seizures), headaches, confusion, or struggling to focus			X
Myocardial infarction (heart attack): pressure or squeezing pain between the shoulder blades, in the chest, jaw, left arm or upper abdomen, shortness of breath, dizziness, fatigue, light-headedness, clammy skin, sweating, indigestion, anxiety, feeling faint and possible irregular heartbeat.			X
Pneumonia (infection in the lungs): chest pain when you breath or cough, confusion, cough which may produce phlegm, fatigue, fever, sweating and shaking chills, nausea, vomiting or diarrhea, shortness of breath		X	
Stroke (bleeding or blood clot in the brain): sudden numbness, weakness or tingling of the face, arm, or leg, particularly on one			X

side of the body, sudden headache, blurry vision, difficulty swallowing or speaking, or lethargy, dizziness, fainting, vomiting, trouble understanding, trouble with walking and loss of balance			
Anal fistula (abnormal connection between the anus and another part of your body): pain and swelling around the anus, pain with bowel movements, bleeding, bloody or foul-smelling discharge from the anus, fever, chills	X		
Pancreatitis (inflammation of the pancreas): abdominal pain that lasts or gets worse when you lie down, nausea, vomiting	X		
Liver injury (including liver failure): yellowing of the skin or eyes, dark urine, abdominal pain, nausea, vomiting, loss of appetite, itching, bruising, weight loss. Can be fatal.			X
Hepatitis cholestatic (decrease in bile flow from the liver): yellow skin or eyes	X		
Pulmonary Embolism (blood clot in the lungs): sharp chest pain, coughing up blood, sudden shortness of breath			X
Pleural effusion (build-up of fluid around the lung): chest pain, dry cough, fever, difficulty breathing, shortness of breath			X
Osteonecrosis (bone damage in the jaw): pain in the mouth, teeth and/or jaw, swelling or sores inside the mouth, numbness, or a feeling of heaviness in the jaw, or loosening of a tooth		X	
Wound complication: a wound that does not heal		X	
Thyroiditis (swelling or inflammation of the thyroid gland): feelings of worry, irritability, anxiety or nervousness, trouble sleeping, fatigue, weight loss, increased appetite, shaking		X	
VERY RARE			
Artery Dissection (separation of the layers of an artery wall): sudden severe pain in the back, chest or abdomen		X	
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,		X	

problems swallowing, hoarse voice, unusual pulsing in your chest or abdomen.			
UNKNOWN			
QT Prolongation (an abnormal heart signal): irregular heartbeat, fainting, loss of consciousness			X
Posterior reversible encephalopathy syndrome: headache, confusion, seizures (fits), visual problems			X
Dysphagia: Difficulty swallowing that can cause food or liquid to get into your lungs, problems with your esophagus		X	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to 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.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 healthcare professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store at 15°C to 25°C. Keep out of reach and sight of children.

If you want more information about CABOMETYX:

- 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 at www.ipsen.ca or by calling 1-855-215-2288.

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