

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. You can report side effects to your doctor, or directly at www.tga.gov.au/reporting-problems.

CABOMETYX®

20mg, 40mg and 60 mg Tablets
cabozantinib

Consumer Medicine Information

WHAT IS IN THIS LEAFLET

This leaflet answers some common questions about CABOMETYX.

This leaflet does not contain all the available information. It does not take the place of talking to your doctor or pharmacist.

All medicines have risks and benefits. Your doctor has weighed the risks of you taking CABOMETYX against the benefits they expect it will have for you.

If you have any concerns about taking this medicine, ask your doctor or pharmacist.

Keep this leaflet with the medicine.

You may need to read it again.

WHAT CABOMETYX IS USED FOR

CABOMETYX is used to treat:

- advanced stages of a type of kidney cancer called renal cell carcinoma (RCC)
- liver cancer in adults who have been previously treated with a specific anticancer medicine (sorafenib)
- a type of thyroid cancer called differentiated thyroid cancer (DTC), in adults and children 12 years of age and older, that has spread (locally advanced or metastatic), and,
 - has progressed after treatment with a medicine called VEGFR targeted treatment, and,
 - when the DTC can no longer be treated with radioactive iodine, or patients are not able to receive radioactive iodine treatment.

CABOMETYX may also be given in combination with another medicine called nivolumab to treat advanced kidney cancer (RCC). It is important that you also read the Consumer Medicine Information of nivolumab.

It contains the active ingredient cabozantinib (S)-malate.

It is a multi-kinase inhibitor.

It works by blocking the action of proteins called receptor tyrosine kinases (RTKs), which are involved in the growth of cells and the development of new blood vessels that supply them. These proteins can be present in high amounts in cancer cells, and by blocking their action CABOMETYX can slow down the rate at which the tumour grows and help to cut off the blood supply that the cancer needs.

Ask your doctor if you have any questions about why this medicine has been prescribed for you.

Your doctor may have prescribed it for another reason.

This medicine is available only with a doctor's prescription.

BEFORE YOU TAKE CABOMETYX

When you must not take it

Do not take CABOMETYX if you have an allergy to:

- cabozantinib, the active ingredient in CABOMETYX
- any of the other ingredients listed at the end of this leaflet under Product Description

Some of the symptoms of an allergic reaction may include:

- shortness of breath
- wheezing or difficulty breathing
- swelling of the face, lips, tongue or other parts of the body
- rash, itching or hives on the skin

CABOMETYX tablets contains lactose.

If you have been told by your doctor that you have intolerance to some sugars, tell your doctor before taking Cabometyx.

Do not take this medicine after the expiry date printed on the pack or if the packaging is torn or shows signs of tampering.

If it has expired or is damaged, return it to your pharmacist for disposal.

If you are not sure whether you should start taking this medicine, talk to your doctor.

Before you start to take it

Tell your doctor if you have allergies to any other medicines, foods, preservatives or dyes.

Tell your doctor if you are pregnant or plan to become pregnant or are breastfeeding.

You should avoid becoming pregnant while being treated with CABOMETYX.

CABOMETYX should not be taken during pregnancy. Your doctor will discuss the risks with you.

If you or your partner could become pregnant, you must use a safe and effective form of contraception (such as a condom or coil) to avoid becoming pregnant while you are being treated with CABOMETYX. You should also do this for at least 4 months after stopping treatment. Discuss with your doctor what may be appropriate contraception for you.

Tell your doctor if you are taking oral contraceptives.

If you take CABOMETYX whilst using oral contraceptives, the oral contraceptives may be ineffective.

You should not breastfeed while taking CABOMETYX and for at least 4 months after treatment has finished, as cabozantinib and/or its metabolites may be excreted in breast milk and be harmful to your child.

Tell your doctor if you or your partner plan to become pregnant in the future. CABOMETYX may affect your fertility.

CABOMETYX is not recommended for children or adolescents for treatment of liver or kidney cancer.

CABOMETYX can be used to treat children and adolescents 12 years of age or older with thyroid cancer. It is not known if CABOMETYX is safe and effective in children younger than 12 years of age

Tell your doctor if you:

- have high blood pressure
- have, or have had, an aneurysm (enlargement and weakening of a blood vessel wall) or a tear in a blood vessel wall
- have diarrhoea
- have a recent history of significant bleeding
- have had surgery within the last month (or if surgical procedures are planned), including dental surgery
- have inflammatory bowel disease (for example, Crohn's disease or ulcerative colitis, diverticulitis, or appendicitis)
- have a recent history of blood clot in the leg, stroke, or heart attack
- have liver or kidney disease.
- have a pre-existing heart condition, slow heart rate or are taking medicine to prevent abnormal heart rhythm.

If you have not told your doctor or pharmacist about any of the above, tell them before you start taking CABOMETYX.

You may need treatment for them, or your doctor may decide to change your dose of CABOMETYX, or stop treatment altogether.

Taking other medicines

Tell your doctor or pharmacist if you are taking any other medicines, including any that you get without a prescription from your pharmacy, supermarket or health food shop.

This is because CABOMETYX can affect the way some other medicines work. Also, some medicines can affect the way CABOMETYX works. This could mean that your doctor needs to change the dose(s) that you take.

You should tell your doctor about every medicine, but in particular if taking:

- 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 to treat angina pectoris (chest pain owing to inadequate supply to the heart) such as ranolazine
- 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 and dabigatran etexilate
- Medicines to treat high blood pressure or other heart conditions, such as ambrisentan, 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 prevent transplant rejection (ciclosporin) and ciclosporin-based regimens in rheumatoid arthritis and psoriasis
- Medicines used for contraception such as oral contraceptives

You may need to use different amounts of your medicine. Your doctor will be able to advise you. Your doctor and pharmacist will have a complete list of medicines to be careful of and to avoid while taking CABOMETYX.

You should tell your doctor if you are taking oral contraceptives.

If you take CABOMETYX whilst using oral contraceptives, the oral contraceptives may be ineffective.

HOW TO TAKE CABOMETYX

Follow all directions given to you by your doctor or pharmacist carefully.

They may differ from the information contained in this leaflet.

If you do not understand the instructions, ask your doctor or pharmacist for help.

How much to take

The usual dose of CABOMETYX is 60 mg taken once a day.

When CABOMETYX is given in combination with nivolumab for the treatment of advanced kidney cancer, the recommended dose of CABOMETYX is 40 mg once a day.

Your doctor will decide on the right dose for you.

Ask your doctor or pharmacist if you are unsure of the correct dose for you.

They will tell you exactly how much to take.

How to take it

Swallow the tablet whole with a full glass of water. Do not crush the tablets.

CABOMETYX should not be taken with food. You should not eat anything for at least 2 hours before taking CABOMETYX and for 1 hour after taking the medicine. Avoid consuming grape-fruit juice or grapefruit-containing products for as long as you are using this medicine, as they may increase the levels of CABOMETYX in your blood.

When to take CABOMETYX

Take your medicine at about the same time each day.

Taking it at the same time each day will have the best effect. It will also help you remember when to take it.

When CABOMETYX is given in combination with nivolumab, you will first be given nivolumab followed by CABOMETYX.

How long to take CABOMETYX

Continue taking your medicine for as long as your doctor tells you.

Do not stop unless your doctor advises you to stop your treatment.

If you get serious side effects, your doctor may decide to change your dose or stop

treatment earlier than originally planned. Your doctor will tell you if you need your dose adjusted.

If you forget to take it

If there are still 12 hours or more before your next dose is due, then take the missed dose as soon as you remember.

Take the next dose at the normal time.

If your next dose is due in less than 12 hours, then do not take the dose that you have missed. Wait until your next dose, and then continue to take it as you would normally.

Do not take a double dose to make up for the dose that you missed.

This may increase the chance of you getting an unwanted side effect.

If you are not sure what to do, ask your doctor or pharmacist.

If you have trouble remembering to take your medicine, ask your pharmacist for some hints.

If you stop using CABOMETYX

Stopping your treatment may stop the effect of the medicine. Do not stop treatment with CABOMETYX unless you have discussed this with your doctor.

When CABOMETYX is given in combination with nivolumab, please refer to the Consumer Medicine Information of nivolumab in order to understand the use of that medicine.

If you take too much (overdose)

Immediately telephone your doctor or the Poisons Information Centre (telephone Australia 13 11 26 for advice, or go to Accident and Emergency at the nearest hospital, if you think that you or anyone else may have taken too much CABOMETYX. Do this even if there are no signs of discomfort or poisoning. You may need urgent medical attention.

WHILE YOU ARE TAKING CABOMETYX

Things you must do

If you are about to be started on any new medicine, remind your doctor and pharmacist that you are taking CABOMETYX.

Tell any other doctors and pharmacists who treat you that you are taking CABOMETYX.

If you are going to have surgery, tell the surgeon or anaesthetist that you are taking CABOMETYX.

It may affect other medicines used during surgery.

You should also tell your dentist that you are taking CABOMETYX.

It is important for you to practice good mouth care during treatment with CABOMETYX.

If you become pregnant while taking CABOMETYX, tell your doctor immediately.

Do not stop treatment without first discussing it with your doctor.

Keep all of your doctor's appointments so that your progress can be checked.

Things you must not do

Do not take CABOMETYX to treat any other complaints unless your doctor tells you to.

Do not give your medicine to anyone else, even if they have the same condition as you.

Do not stop taking your medicine or lower the dosage without checking with your doctor.

Things to be careful of

Use caution when driving or operating machines.

Treatment with CABOMETYX may make you feel tired or weak and can affect your ability to drive or operate machines.

SIDE EFFECTS

Tell your doctor or pharmacist as soon as possible if you do not feel well while you are taking CABOMETYX

All medicines can have side effects. Sometimes they are serious, most of the time they are not. You may need medical attention if you get some of the side effects.

Do not be alarmed by the following lists of side effects. You may not experience any of them.

The following side effects can be serious and you should tell your doctor immediately or go to a hospital if you experience any of them:

- Symptoms including pain in the abdomen (belly), nausea (feeling sick), vomiting, constipation, or fever. These may be signs of a gastrointestinal perforation, a hole that develops in your stomach or intestine that could be life-threatening.
- Severe or uncontrollable bleeding with symptoms such as: vomiting blood, black stools, bloody urine, headache, coughing up blood.
- Swelling, pain in your hands and feet, or shortness of breath.
- A wound that does not heal.
- Fits, headaches, confusion, or finding it difficult to concentrate. These may be signs of a condition called posterior reversible encephalopathy syndrome (PRES). PRES is rare (it affects less than 1 in 1000 people).
- Feeling drowsy, confused or loss of consciousness. This may be due to liver problems.
- 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. These could be signs of bone damage in the jaw (osteonecrosis).

Tell the doctor if you have any of the following:

Other side effects with CABOMETYX alone:

Very common side effects of CABOMETYX (more than 1 in 10 patients) are:

- Stomach upset, including diarrhoea, nausea, vomiting, constipation, indigestion, abdominal pain
- Blisters, pain of the hands or soles of the feet, rash or redness of the skin

- Decreased appetite, weight loss, altered sense of taste
- Fatigue, weakness, headache, dizziness
- High blood pressure (hypertension)
- Low levels of red blood cells (anaemia)
- Low levels of blood platelets
- Redness, swelling or pain in the mouth or throat, difficulty in speaking, hoarseness, cough
- Changes in blood tests used to monitor general health and function of your organs (including the liver and kidney), low levels of electrolytes (like magnesium, or potassium)
- Shortness of breath
- Reduced thyroid activity; symptoms can include: tiredness, weight gain, constipation, feeling cold and dry skin
- Swelling in your legs and arms
- Pain in the arms, hands, legs or feet
- Low level of albumin in blood

Common side effects of CABOMETYX (may affect up to 1 in 10 patients) are:

- Abscess (collection of pus, with swelling and inflammation)
- Dehydration (lack of fluids)
- Difficulty in swallowing
- Ringing in ears (tinnitus)
- Blood clots in the veins, arteries and lungs
- Low level of white blood cells
- Increased or decreased blood glucose level
- Decrease in levels of calcium, sodium and phosphate in the blood
- Increase in level of potassium in the blood
- Increase in the level of bilirubin in the blood (which may result in jaundice/yellow skin or eyes)
- Increase in amylase levels in the blood
- Increase in lipase levels in the blood
- Increase in cholesterol or triglyceride levels in the blood
- Numbness, tingling, burning sensation or pain in the limbs
- Inflammation of the pancreas
- A painful tear or abnormal connection of the tissues in your body (fistula)
- Gastro-oesophageal reflux disease (bringing up stomach acid)
- Haemorrhoids (piles)
- Dry mouth and pain in the mouth
- Feeling drowsy, confused or loss of consciousness due to liver problems
- Dry skin, severe itching of skin, acne
- Thickening of the outer layer of the skin
- Alopecia (hair loss and thinning), hair colour change
- Pain in arms, legs and joints, muscle spasms
- Protein in urine (seen in tests)
- A burning or stinging sensation of the tongue
- Wound complications

Uncommon side effects of CABOMETYX (between 1 in a 100 and 1 in a 1000 patients) are:

- Stroke
- Fits

- Decrease in bile flow from the liver
- Bone damage in the jaw

Not known (proportion of people affected not known)

- Heart attack
- An enlargement and weakening of a blood vessel wall or a tear in a blood vessel wall (aneurysms and artery dissections)

The following side effects have been reported with CABOMETYX in combination with nivolumab:

Very common side effects (may affect more than 1 in 10 people)

- Reduced thyroid activity; symptoms can include tiredness, weight gain, constipation, feeling cold and dry skin
- Decreased appetite, altered sense of taste
- High blood pressure (hypertension)
- Difficulty in speaking, hoarseness (dysphonia)
- Stomach upset, including diarrhoea, nausea, vomiting, indigestion and abdominal pain
- Redness, swelling or pain in the mouth or throat (stomatitis)
- Skin rash sometimes with blisters, itching, pain of the hands or soles of the feet, rash or redness of the skin
- Fatigue

Common side effects (may affect up to 1 in 10 people)

- Infections of the upper respiratory tract
- Allergic reaction
- Decreased secretion of hormones produced by adrenal glands (glands situated above the kidneys)
- Increased thyroid activity; symptoms can include rapid heart rate, sweating and weight loss
- Dehydration
- Headache
- Inflammation of the nerves (causing numbness, weakness, tingling or burning pain of the arms and legs), dizziness
- Dry eyes
- Blood clots in the blood vessels
- Inflammation of the lungs (pneumonitis, characterised by coughing and difficulty breathing), blood clots in the lung
- Cough and nose bleeding
- Dry mouth, pain in the mouth, constipation and inflammation of the stomach (gastritis)
- Inflammation of the liver (hepatitis)
- Dry skin and severe itching of skin
- Alopecia (hair loss and thinning), hair colour change
- Inflammation of the joints (arthritis) and pain in joints (arthralgia)
- Muscle spasm, muscle weakness and aching muscles
- Kidney failure (including abrupt loss of kidney function), protein in the urine (seen in test)
- Oedema (swelling), pain, chills
- Hypocalcaemia (low levels of calcium as seen in blood tests)

Uncommon side effects (may affect 1 in 100 people)

- Serious lung infection (pneumonia),

- Increase in some white blood cells called eosinophils
- Allergic reactions related to the infusion of the medicine nivolumab
- Inflammation of the pituitary gland situated at the base of the brain (hypophysitis), swelling of the thyroid gland (thyroiditis)
- A temporary inflammation of the nerves that causes pain, weakness and paralysis in the extremities (Guillain Barré syndrome); muscle weakness and tiredness without atrophy (myasthenic syndrome)
- Inflammation of the brain
- Ringing in ears (tinnitus)
- Inflammation of the eye (which causes pain and redness) and blurred vision
- Changes in the rhythm or rate of the heartbeat, fast heart rate, inflammation of the heart muscle
- Fluid around the lungs
- Inflammation of the colon (colitis), inflammation of the pancreas (pancreatitis), intestinal perforation, burning or painful sensation in the tongue (glossodynia), haemorrhoids (piles)
- Skin disease with thickened patches of red skin, often with silvery scales (psoriasis)
- Hives (itchy rash)
- Muscle tenderness or weakness, not caused by exercise (myopathy), bone damage in the jaw, painful tear or abnormal connection of the tissues in your body (fistula)
- Inflammation of the kidney
- Chest pain

Changes in test results

CABOMETYX in combination with nivolumab may cause changes in the results of tests carried out by your doctor. These include:

- Abnormal liver function tests (increased amounts of the liver enzymes aspartate aminotransferase, alanine aminotransferase or alkaline phosphatase in your blood, higher blood levels of the waste product bilirubin)
- Abnormal kidney function tests (increased amounts of creatinine in your blood)
- High (hyperglycaemia) or low (hypoglycaemia) sugar levels in the blood
- A decreased number of red blood cells (which carry oxygen), white blood cells (which are important in fighting infection) or platelets (cells which help the blood to clot)
- Decrease in levels of amount of phosphate
- Increased or decreased amount of calcium or potassium
- Increased or decreased blood levels of magnesium or sodium
- Decrease in body weight

If you get any side effects, talk to your doctor or pharmacist.

This includes any possible side effects not listed in this leaflet.

Ask your doctor or pharmacist to answer any questions you may have.

Tell your doctor or pharmacist if you notice anything else that is making you feel unwell.

AFTER TAKING CABOMETYX

Storage

Keep your medicine in the original container.

If you take it out of its original container it may not keep well.

Store your tablets in a cool, dry place where the temperature stays below 25°C.

Do not store CABOMETYX or any other medicine in the bathroom, near a sink or on a window sill.

Do not leave it in the car.

Heat and dampness can destroy some medicines.

Keep it where children cannot reach it.

A locked cupboard at least one-and-a-half metres above the ground is a good place to store medicines.

Disposal

If your doctor tells you to stop taking this medicine or the expiry date has passed, ask your pharmacist what to do with any medicine that is left over.

Return any unused medicine to your pharmacist.

PRODUCT DESCRIPTION

What it looks like

CABOMETYX 20 mg film-coated tablets are yellow, round with no score, and identified with "XL" on one side and "20" on the other side.

CABOMETYX 40 mg film-coated tablets are yellow, triangle shaped with no score, and identified with "XL" on one side and "40" on the other side.

CABOMETYX 60 mg film-coated tablets are yellow, oval shaped with no score, and identified with "XL" on one side and "60" on the other side.

CABOMETYX tablets are available in a plastic bottle with 30 tablets.

The bottle contains three silica gel desiccant canisters. Keep the canisters in the bottle and do not swallow the desiccant canisters.

Ingredients

Active ingredient:

- Cabozantinib as cabozantinib (S)-malate

Excipient Ingredients:

- microcrystalline cellulose,
- lactose,
- hypromellose,
- croscarmellose sodium,
- colloidal anhydrous silica
- magnesium stearate.
- hypromellose,
- titanium dioxide,
- triacetin
- iron oxide yellow

This medicine does not contain gluten, tartrazine or any other azo dyes.

SPONSOR

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AUST R 283800

CABOMETYX 40 mg film coated tablet:
AUST R 283801

CABOMETYX 60 mg film coated tablet:
AUST R 283799

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