Cabozantinib (Cometriq®, Cabometyx™)

**Pronounced:** ka-boe-zan-ti-nib

**Classification:** Tyrosine Kinase Inhibitor

### About Cabozantinib (Cometriq®, Cabometyx™)

A kinase is an enzyme that promotes cell growth. There are many types of kinases, which control different phases of cell growth. By blocking a particular enzyme from working, this medication can slow the growth of cancer cells.

Cabozantinib is a type of targeted therapy called a tyrosine kinase inhibitor that blocks a few targets including VEGF, MET, RET, and ROS. This means it works by targeting receptors present on the cancer cells. By blocking these targets on cancer cells, tumor growth and angiogenesis (the development of a blood supply to the tumor) are blocked.

### How to Take Cabozantinib

Cabozantinib comes in both capsule and tablet form, both in several dosage strengths. You should never substitute capsules for tablets or tablets for capsules. It is taken once a day on an empty stomach. Do not eat for 2 hours before, or 1 hour after the dose. Swallow the capsules or tablets whole with a full glass (at least 8 ounces) of water; do not open, break or chew the capsules or tablets. Do not take a missed dose within 12 hours of the next dose. Do not take 2 doses at once to make up for a missed dose.

It is important to make sure you are taking the correct amount of medication every time. Before every dose, check that what you are taking matches what you have been prescribed.

The blood levels of this medication can be affected by certain foods and medications, so they should be avoided. Your dose may be altered if you are taking any of these medications. These include: grapefruit, grapefruit juice, ketoconazole, posaconazole, voriconazole rifampin, phenytoin, phenobarbital, St. John’s wort, and carbamazepine. Be sure to tell your healthcare provider about all medications and supplements you take. There is an increased risk for liver toxicity and adrenal insufficiency when taking this medication with nivolumab. Your provider will monitor you for these side effects.

### Storage and Handling

Store your medication in the original, labeled container at room temperature and in a dry location (unless otherwise directed by your healthcare provider or pharmacist). This medication should not be stored in a pillbox. Keep containers out of reach of children and pets.

If a caregiver prepares your dose for you, they should consider wearing gloves or pour the pills directly from their container into the cap, a small cup, or directly into your hand. They should avoid touching the pills. They should always wash their hands before and after giving you the medication. Pregnant or nursing women should not prepare the dose for you. Ask your oncology team where to return any unused medication for disposal. Do not flush down the toilet or throw it in the trash.

### Where do I get this medication?

Cabozantinib is available through select specialty pharmacies. Your oncology team will work with your prescription drug plan to identify an in-network specialty pharmacy for distribution of this medication and shipment directly to your home.

### Insurance Information

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This medication may be covered under your prescription drug plan. Patient assistance may be available to qualifying individuals depending upon prescription drug coverage. Co-pay cards, which reduce the patient co-pay responsibility for eligible commercially (non-government sponsored) insured patients, may also be available. Your care team can help you find these resources, if they are available.

Possible Side Effects

There are a number of things you can do to manage the side effects of cabozantinib. Talk to your care team about these recommendations. They can help you decide what will work best for you. These are some of the most common or important side effects:

**Diarrhea**

Diarrhea can be a serious side effect that can lead to dehydration and other gastrointestinal side effects. Notify your healthcare provider immediately if you are experiencing an increase in the frequency of bowel movements or if your bowel movements become loose.

**Fatigue**

Fatigue is very common during cancer treatment and is an overwhelming feeling of exhaustion that is not usually relieved by rest. While on cancer treatment, and for a period after, you may need to adjust your schedule to manage fatigue. Plan times to rest during the day and conserve energy for more important activities. Exercise can help combat fatigue; a simple daily walk with a friend can help. Talk to your healthcare team for helpful tips on dealing with this side effect.

**Nausea and/or Vomiting**

Talk to your oncology care team so they can prescribe medications to help you manage nausea and vomiting. In addition, dietary changes may help. Avoid things that may worsen the symptoms, such as heavy or greasy/fatty, spicy or acidic foods (lemons, tomatoes, oranges). Try saltines, or ginger ale to lessen symptoms.

Call your oncology care team if you are unable to keep fluids down for more than 12 hours or if you feel lightheaded or dizzy at any time.

**Decrease in Appetite or Taste Changes**

Nutrition is an important part of your care. Cancer treatment can affect your appetite and, in some cases, the side effects of treatment can make eating difficult. Ask your oncology care team about nutritional counseling services at your treatment center to help with food choices.

- Try to eat five or six small meals or snacks throughout the day, instead of 3 larger meals.
- If you are not eating enough, nutritional supplements may help.
- You may experience a metallic taste or find that food has no taste at all. You may dislike foods or beverages that you liked before receiving cancer treatment. These symptoms can last for several months or longer after treatment ends.
- Avoid any food that you think smells or tastes bad. If red meat is a problem, eat chicken, turkey, eggs, dairy products, and fish without a strong smell. Sometimes cold food has less of an odor.
- Add extra flavor to meat or fish by marinating it in sweet juices, sweet and sour sauce, or dressings. Use seasonings like basil, oregano, or rosemary to add flavor. Bacon, ham, and onion can add flavor to vegetables.

**Hand Foot Syndrome**

Hand foot syndrome (HFS) is a skin reaction that appears on the palms of the hands and/or the soles of the feet, as a result of certain chemotherapy agents being absorbed by the skin cells. HFS can begin as a mild tingling, numbness, pins-and-needles feeling, redness or pain or swelling of the hands and/or feet. This can then progress to painful swelling, blistering, or peeling skin that can interfere with your ability to do normal activities. Be sure to let your oncology team know right away if you notice these symptoms, as they may need to adjust the chemotherapy dose or take a break to allow the skin to heal. Some tips to help prevent HFS include:

- Keep hands and feet clean and dry.
- Avoid tight shoes or socks.
- Avoid activities that put pressure on the palms or soles for 1 week after treatment.
- Apply an alcohol-free moisturizer liberally and often. (Avoid moisturizers with perfumes or scents)
- Avoid very hot water for baths and showers.

High Blood Pressure
This medication can cause high blood pressure (hypertension). Patients should have their blood pressure checked regularly during therapy. Any hypertension should be treated appropriately. If hypertension cannot be controlled, the medication may be stopped. Report any headaches, vision changes, or dizziness to your oncology care team.

Mouth Ulcers (Mucositis)
Certain cancer treatments can cause sores or soreness in your mouth and/or throat. Notify your oncology care team if your mouth, tongue, inside of your cheek or throat becomes white, ulcerated, or painful. Performing regular mouth care can help prevent or manage mouth sores. If mouth sores become painful, your doctor or nurse can recommend a pain reliever.

- Brush with a soft-bristle toothbrush or cotton swab twice a day.
- Avoid mouthwashes that contain alcohol. A baking soda and/or salt with warm water mouth rinse (2 level teaspoons of baking soda or 1 level teaspoon of salt in an eight-ounce glass of warm water) is recommended 4 times daily.
- If your mouth becomes dry, eat moist foods, drink plenty of fluids (6-8 glasses), and suck on sugarless hard candy.
- Avoid smoking and chewing tobacco, drinking alcoholic beverages, and citrus juices.

Less common, but important side effects can include:
- GI Perforations and Fistulas: This medication can cause a tear in the intestinal wall, (gastrointestinal perforation) or a fistula (an abnormal connection between two parts of your body). Signs of this can include: new or worsening pain in the abdomen, new abdominal swelling, chills, fever, constipation, nausea, vomiting, or coughing, gagging and choking, especially when eating or drinking. If you experience any of these, contact your healthcare provider immediately or go to the emergency room.
- Bleeding: Cabozantinib can cause abnormal bleeding. Contact your health care team immediately if you experience any bleeding, including: coughing up blood or blood clots, vomiting blood, or if your vomit looks like coffee grounds, red or black stools, heavier than normal menstrual bleeding, or other unusual or heavy bleeding.
- Blood Clots, Stroke, and Heart Attack: This medication can increase the risk of blood clots, stroke, and heart attack. If you experience symptoms of these problems, you should contact your healthcare provider immediately or go to an emergency room. Symptoms can include: swelling, redness or pain in an extremity, chest pain or pressure, pain in your arm, back, neck or jaw, shortness of breath, numbness or weakness on one side of the body, trouble talking, confusion or mental status changes. Let your care team know if you have a history of previous blood clots, as you may require preventive medication.
- Wound Healing Complications This medication can lead to slower or incomplete wound healing, such as a surgical wound not healing or staying closed. Therefore, it is recommended that the medication be discontinued 28 days prior to any surgery. In addition, any surgical incision should be fully healed prior to starting or restarting the medication. If you have a surgical wound that has not healed or begins to have signs of infection (redness, swelling, warmth), report this to your healthcare team.
- Proteinuria: This medication can cause increased protein in your urine. Your healthcare team will monitor your kidney function while you are being treated with cabozantinib. If you experience swelling of your hands, arm, legs or feet, inform your healthcare team immediately. This side effect is more common in patients who take the capsule form of this medication.
- Posterior Reversible Encephalopathy Syndrome (PRES): PRES is a rare, reversible neurological disorder that can occur with the use of cabozantinib. Symptoms of PRES include seizure, high blood pressure, headache, confusion, fatigue, confusion, blindness and other visual or neurological disturbances. If you experience any of these symptoms, contact your care team or go to the emergency room immediately.
- Hair Changes: This medication can cause your hair to turn gray, lose its color, or change color.
- **Electrolyte and Blood Count Abnormalities**: This medication can affect the normal levels of LFTs, calcium, phosphate, white blood cells, and platelets in your body. Your levels will be monitored using blood tests. If your levels become too low, your care team may prescribe specific electrolytes or blood products to be given. Do not take any supplements without first consulting with your care team.

- **Osteonecrosis of the Jaw**: Osteonecrosis of the jaw (ONJ) is a rare side effect that is more common in patients who take the capsule formulation of this medication. It is important that you know about it and take steps to protect your dental health. The maxilla (upper jaw bone) and mandible (lower jaw bone) are normally covered by gum tissue. In the case of ONJ, this tissue is gone and the bone is exposed. Typical symptoms associated with ONJ are: pain, swelling or infection of the gums, loosening of the teeth, exposed bone (often at the site of a previous tooth extraction). Some patients may report numbness or tingling in the jaw or a “heavy” feeling jaw. ONJ may have no symptoms for weeks or months and may only be recognized by the presence of exposed bone. ONJ most often occurs soon after a dental procedure, though not always. Stop treatment with cabozanitib at least 28 days prior to any dental procedures.
  - Prior to starting therapy, you should have a complete dental exam, cleaning, and removal of any teeth in poor health.
  - Dentures should be checked for proper fit.
  - Brush your teeth after meals and at bedtime with a soft brush. Floss gently once a day. If your gums bleed, talk with your healthcare team to see if you can continue to floss.
  - Check your teeth and gums in a mirror daily for any sores, swelling, loose teeth, pain or numbness, or other changes and report these to your dentist or oncology team immediately.

- **Thyroid Issues**: This medication can affect how your thyroid works. Your thyroid function will be checked before you start this medication and during treatment. Notify your provider if you have trouble sleeping, weight loss or gain, muscle weakness, fatigue or hyperactivity, anxiety, irritability, nervousness, feeling too warm or too cold, or high heart rate.

**Reproductive Concerns**

Exposure of an unborn child to this medication could cause birth defects, so you should not become pregnant or father a child while on this medication. Effective birth control is necessary during treatment and for at least 4 months after treatment. Even if your menstrual cycle stops or you believe you are not producing sperm, you could still be fertile and conceive. It is recommended you do not breastfeed during treatment and for 4 months after the final dose.