Package leaflet: Information for the patient

COMETRIQ 20 mg hard capsules
COMETRIQ 80 mg hard capsules
cabozantinib

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What COMETRIQ is and what it is used for
2. What you need to know before you take COMETRIQ
3. How to take COMETRIQ
4. Possible side effects
5. How to store COMETRIQ
6. Contents of the pack and other information

1. What COMETRIQ is and what it is used for

What COMETRIQ is
COMETRIQ is a cancer medicine that contains the active substance cabozantinib (*S*)-malate.
It is a medicine used to treat medullary thyroid cancer, a rare type of thyroid cancer, that cannot be removed by surgery or that has spread to other parts of the body.

How COMETRIQ works
COMETRIQ blocks 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 COMETRIQ can slow down the rate at which the tumour grows and help to cut off the blood supply that the cancer needs.
COMETRIQ may slow or stop the growth of medullary thyroid cancer. It may help shrink tumours associated with this type of cancer.

2. What you need to know before you take COMETRIQ

Do not take COMETRIQ
- if you are allergic to cabozantinib or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

Talk to your doctor or pharmacist before taking COMETRIQ 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 coughing up blood or significant bleeding
- have had surgery within the last month (or if surgical procedures are planned), including dental procedures
- have had radiotherapy in the last 3 months
- have inflammatory bowel disease (for example, Crohn's disease or ulcerative colitis or diverticulitis)
- have been told that your cancer has spread to your airway or oesophagus
- have a recent history of blood clot in the leg, stroke, or heart attack
- have heart failure (can include symptoms like shortness of breath, feeling tired, fainting, swollen ankles and legs)
- are taking medicines to control your heart rhythm, have a slow heart rate, have problems with your heart or have problems with the levels of calcium, potassium or magnesium in your blood
- have liver or kidney disease.

Tell your doctor if any of these affect you. You may need treatment for them, or your doctor may decide to change your dose of COMETRIQ, or stop treatment altogether. See also section 4 "*Possible side effects"*.

You should also tell your dentist that you are taking COMETRIQ. It is important for you to practice good mouth care during treatment with COMETRIQ.

Children and adolescents

COMETRIQ is not recommended for children or adolescents. The effects of COMETRIQ in people younger than 18 years old are not known.

Other medicines and COMETRIQ

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. This is because COMETRIQ can affect the way some other medicines work. Also, some medicines can affect the way COMETRIQ works. This could mean that your doctor needs to change the dose(s) that you take.

- Medicines used to 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 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 to treat depression or depression-related conditions such as anxiety
- Medicines used to thin the blood, such as warfarin and dabigatran etexilate
- Medicines used to treat high blood pressure or other heart conditions, such as aliskiren, ambrisentan, digoxin, talinolol, 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 ritonavir, maraviroc and emtricitabine
- Medicines used to treat viral infections such as efavirenz
- Medicines used to prevent transplant rejection (cyclosporine) and cyclosporine-based regimens in rheumatoid arthritis and psoriasis

Oral contraceptives
If you take COMETRIQ whilst using oral contraceptives, the oral contraceptives may be ineffective. You should also use a barrier contraceptive (e.g. condom or diaphragm) whilst taking COMETRIQ and for at least 4 months after treatment has finished.

Taking COMETRIQ with food

Avoid consuming grapefruit-containing products for as long as you are using this medicine, as it may increase the levels of COMETRIQ in your blood.

Pregnancy, breast-feeding, and fertility

Avoid becoming pregnant while being treated with COMETRIQ. If you or your partner could become pregnant, use adequate contraception during treatment and for at least 4 months after treatment has finished. Talk to your doctor about which methods of contraception are appropriate while you are taking COMETRIQ. See section 2.

Tell your doctor if you or your partner become pregnant or plan to become pregnant while you are being treated with COMETRIQ.

Talk to your doctor BEFORE taking COMETRIQ if you or your partner are considering or planning to have a baby after your treatment has finished. There is a possibility your fertility could be affected by treatment with COMETRIQ.

Women taking COMETRIQ should not breast feed during treatment 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.

Driving and using machines

Use caution when driving or using machines. Keep in mind that treatment with COMETRIQ may make you feel tired or weak.

COMETRIQ contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per capsule, that is to say essentially "sodium-free".

3. How to take COMETRIQ

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

You should continue to take this medicine until your doctor decides to stop your treatment. If you experience serious side effects, your doctor may decide to change your dose or stop treatment earlier than originally planned. Your doctor will determine if you need your dose adjusted, particularly during the first eight weeks of therapy with COMETRIQ.

COMETRIQ should be taken once a day. Depending on the dose you were prescribed, the number of capsules to take are as follows:

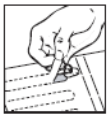
- 140 mg (1 orange 80 mg capsule and 3 grey 20 mg capsules)
- 100 mg (1 orange 80 mg capsule and 1 grey 20 mg capsule)
- 60 mg (3 grey 20 mg capsules)

Your doctor will decide on the right dose for you.

Your capsules will come in a blister card organised by prescribed dose. Each blister card has enough capsules to last for seven days (one week). Your capsules are also available as a 28 day pack, which contains enough capsules to last for 28 days, in 4 blister cards with seven days of capsules on each card.

Each day, take all the capsules across the row. More information on the blister cards including how many capsules you will take and how many capsules there are in total in each blister card are described below in

section 6. To help you remember your doses, write the date when you took your first dose in the space next to the capsules. To remove the capsules for your dose:

1. Push in tab
2. Peel paper backing 
3. Push capsule through foil

COMETRIQ should **not** be taken with food. You should not eat anything for at least 2 hours before taking COMETRIQ and for 1 hour after taking the medicine. Swallow the capsules one at a time with water. Do not open them.

If you take more COMETRIQ than you should
If you have taken more COMETRIQ than you have been instructed to, talk to a doctor or go to the hospital with the capsules and this leaflet straight away.

If you forget to take COMETRIQ
- 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. Take your next dose at the normal time.

If you stop using COMETRIQ
Stopping your treatment may stop the effect of the medicine. Do not stop treatment with COMETRIQ unless you have discussed this with your doctor. If you have any further questions on the use of this medicine, ask your doctor.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. If you get side effects, your doctor may tell you to take COMETRIQ at a lower dose. Your doctor may also prescribe other medicines to help control your side effects.

Tell your doctor straight away if you notice any of the following side effects – you may need urgent medical treatment:
- Symptoms including pain in the abdomen, nausea, 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.
- Swelling, pain in your hands and feet, or shortness of breath.
- A wound that does not heal.
- Vomiting or coughing up blood, which may be bright red or look like coffee grounds.
- 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).
- Seizures, headaches, confusion, or finding it difficult to concentrate. These may be signs of a condition called posterior reversible encephalopathy syndrome (PRES). PRES is uncommon (it affects less than 1 in 100 people).
- Diarrhoea that is severe and does not seem to be settling.

Other side effects include:

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

- Stomach upset, including diarrhoea, nausea, vomiting, constipation, indigestion, and abdominal pain
- Difficulty in swallowing
- Blister, pain of the hands or soles of the feet, rash or redness of the skin, dry skin
- Decreased appetite, weight loss, altered sense of taste
- Fatigue, weakness, headache, dizziness
- Hair colour changes (lightening), hair loss
- Hypertension (increase in blood pressure)
- Redness, swelling or pain in the mouth or throat, difficulty in speaking, hoarseness
- Changes in blood tests used to monitor general health and the liver, low levels of electrolytes (like magnesium, calcium or potassium)
- Low level of platelets
- Joint pain, muscle spasms
- Swollen lymph glands
- Pain in the arms, hands, legs or feet

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

- Anxiety, depression, confusion
- Generalised pain, chest or muscle pain, ear pain, ringing in ears
- Weakness or reduced sensation or tingling in the limbs
- Chills, tremors
- Dehydration
- Inflammation of the abdomen or pancreas
- Inflammation of the lips and corners of the mouth
- Inflammation at the root of your hair, acne, blisters (on parts of your body other than the hands or feet)
- Swelling in the face and in other parts of the body
- Loss or change of taste
- Hypotension (decrease in blood pressure)
- Atrial fibrillation (a fast and erratic heartbeat)
- Lightening of skin, flakey skin, unusual pale skin
- Abnormal hair growth
- Haemorrhoids
- Pneumonia (lung infection)
- 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
- Reduced thyroid activity; symptoms can include: tiredness, weight gain, constipation, feeling cold and dry skin
- Low level of white blood cells
- Decrease in level of phosphate in the blood
- Tear or hole or bleeding in your stomach or intestine, inflammation or tear of anus, bleeding in lungs or trachea (airway)
- An abnormal connection of the tissue in your digestive system; symptoms can include severe or persistent stomach ache
- Abnormal connection of the tissue in your trachea (airway), oesophagus, or lungs
- Abscess (collection of pus, with swelling and inflammation) in the abdomen or pelvis area or in your teeth/gums
- Blood clots in the blood vessels and the lungs
- Stroke
- Heart failure (can include symptoms like shortness of breath, feeling tired, fainting, swollen ankles and legs)

- Fungal infection that can be in the skin, mouth, or genitals
- Wounds that have difficulties healing
- Protein or blood in the urine, gallstones, painful urination
- Blurred vision
- Increase in the level of bilirubin in your blood (which may result in jaundice/yellow skin or eyes)
- Decrease in the levels of protein in your blood (albumin)
- Abnormal kidney function tests (increased amounts of creatinine in your blood)
- Increased level of the serum protein known as lipase.

Uncommon side effects (may affect 1 in 100 people)

- Inflammation of the oesophagus; symptoms can include heartburn, chest pain, feeling sick, altered taste, bloating, belching and indigestion
- Infection and inflammation in the lung, collapse of lung
- Skin ulcers, cysts, red spots on the face or thighs
- Facial pain
- Changes in test results that measure blood clotting or blood cells
- Loss of coordination in your muscles, damage to skeletal muscles
- Loss of attention, loss of consciousness, changes in speech, delirium, abnormal dreams
- Chest pain due to blockage in arteries, rapid heartbeat
- Liver damage, kidney failure
- Impaired hearing
- Inflammation in the eye, cataracts
- Clot/embolus that travelled through your arteries and become stuck
- Stopping menstruation, vaginal bleeding
- A condition called posterior reversible encephalopathy syndrome (PRES) which has symptoms such as seizures, headaches, confusion, or finding it difficult to concentrate
- Severe increase in blood pressure (hypertensive crisis)
- Collapsed lung with air trapped in the space between the lung and chest, often causing shortness of breath (pneumothorax).

Not Known (side effects with unknown frequency)

- Heart attack
- An enlargement and weakening of a blood vessel wall or a tear in a blood vessel wall (aneurysms and artery dissections)
- Inflammation of the blood vessels in the skin (cutaneous vasculitis).

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system (see details below). By reporting side effects, you can help provide more information on the safety of this medicine.

United Kingdom (Great Britain)
Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

5. How to store COMETRIQ

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the blister cards and carton after EXP. The expiry date refers to the last day of that month.

Do not store above 25ºC. Store in the original package in order to protect from moisture.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What COMETRIQ contains

The active substance is cabozantinib (*S*)-malate.

The COMETRIQ 20 mg hard capsules contain cabozantinib (*S*)-malate equivalent to 20 mg of cabozantinib.
The COMETRIQ 80 mg hard capsules contain cabozantinib (*S*)-malate equivalent to 80 mg of cabozantinib.

The other ingredients are:

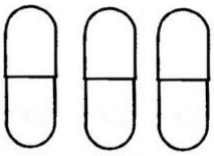
- **Capsule contents:** microcrystalline cellulose, croscarmellose sodium, sodium starch glycolate, silica colloidal anhydrous, and stearic acid (see section 2 " COMETRIQ contains sodium")
- **Capsule shell:** gelatin, and titanium dioxide (E171)
  - The 20 mg capsules also contain black iron oxide (E172)
  - The 80 mg capsules also contain red iron oxide (E172)
- **Printing ink:** shellac glaze, black iron oxide (E172), and propylene glycol

What COMETRIQ looks like and contents of the pack

COMETRIQ 20 mg hard capsules are grey and have "XL184 20mg" printed on one side.
COMETRIQ 80 mg hard capsules are orange and have "XL184 80mg" printed on one side.

COMETRIQ hard capsules are packaged in blister cards organised by prescribed dose. Each blister card contains enough medicine for 7 days. Each row of the blister card contains the daily dose.

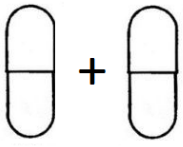
The 60 mg daily dose blister card contains twenty-one 20 mg capsules as 7 daily doses in total. Each daily dose is given in one row and contains three 20 mg capsules:



= 60 mg

three grey 20 mg

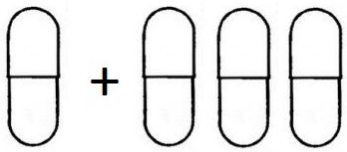
The 100 mg daily dose blister card contains seven 80 mg capsules and seven 20 mg capsules as 7 daily doses in total. Each daily dose is provided in one row and contains one 80 mg capsule and one 20 mg capsule:



= 100 mg

one orange 80 mg + one grey 20 mg

The 140 mg daily dose blister card contains seven 80 mg capsules and twenty one 20 mg capsules as 7 doses in total. Each daily dose is provided in one row and contains one 80 mg capsule and three 20 mg capsules:



= 140 mg

one orange 80 mg + three grey 20 mg

COMETRIQ hard capsules are also available in 28 day packs:
84 capsules (4 blister cards of 21 x 20 mg) (60 mg/day dose)
56 capsules (4 blister cards of 7 x 20 mg and 7 x 80 mg) (100 mg/day dose)
112 capsules (4 blister cards of 21 x 20 mg and 7 x 80 mg) (140 mg/day dose)

Each 28 day pack contains enough medicine for 28 days.

Marketing Authorisation Holder

Ipsen Pharma
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75015 Paris
France

Manufacturer

Catalent Germany Schorndorf GmbH
Steinbeisstr. 1 und 2
73614 Schorndorf
Germany

Tjoapack Netherlands B.V.
Nieuwe Donk 9
4879 AC Etten-Leur
The Netherlands

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder.

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This leaflet was last revised in April 2026

Other sources of information

Is this leaflet hard to see or read? Please phone +44 (0) 1753 627777 and ask for help.