



## Information for the patient

### Cabonni 20 mg / 80mg hard capsules

### Cabozantinib (S)-malate

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. See the end of section 4 for how to report side effects.

**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, pharmacist or nurse.
- 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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

#### What is in this leaflet

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

#### 1. What Cabonni is and what it is used for

##### What Cabonni is and What Cabonni is used for

Cabonni 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.

Cabonni may slow or stop the growth of medullary thyroid cancer. It may help shrink tumours associated with this type of cancer.

##### How Cabonni works

Cabozantinib inhibits the tyrosine kinase activity of RET, MET, VEGFR-1, -2 and -3, KIT, TRKB, FLT-3, AXL, ROS1, TYRO3, MER, and TIE- 2. These receptor tyrosine kinases are involved in both normal cellular function and pathologic processes such as oncogenesis, metastasis, tumor angiogenesis, drug resistance, and maintenance of the tumor microenvironment.

If you have any questions about how Cabonni works or why this medicine has been prescribed for you, ask your doctor, pharmacist or nurse.

#### 2. What you need to know before you take Cabonni

##### Do not take Cabonni

- 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 Cabonni if you:

- have high blood pressure
- 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
- 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 severe liver or kidney disease.

Look out for these while you are taking Cabonni. See 'Side effects' in section 4 for more information.

##### Children and adolescents

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

##### Other medicines and Cabonni

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

- 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 and ranolazine
- Steroids used to reduce inflammation or treat a number of different diseases of the immune system
- 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
- Medicines to treat high blood pressure or other heart conditions, such as aliskiren, ambrisentan, dabigatran etexilate, 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 Cabonni whilst using oral contraceptives, the oral contraceptives may be ineffective. You should also use a barrier contraceptive (e.g. condom or diaphragm) whilst taking Cabonni and for at least 4 months after treatment has finished.

##### Cabonni with food and drink

You should not take Cabonni with food. You should not eat anything for at least 2 hours before taking Cabonni and for 1 hour after taking the medicine. Avoid consuming grapefruit-containing products for as long as you are using this medicine, as it may increase the levels of Cabonni in your blood.

##### Pregnancy, breast-feeding, and fertility

Avoid becoming pregnant while being treated with Cabonni. 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 Cabonni. See section 2.

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

Talk to your doctor before taking Cabonni 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 Cabonni.

Women taking Cabonni 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 Cabonni may make you feel tired or weak.

#### 3. How to take Cabonni

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor, pharmacist or nurse 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 Cabonni.

##### How much to take

Cabonni 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.

##### How to take

Cabonni should not be taken with food. You should not eat anything for at least 2 hours before taking Cabonni 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 Cabonni than you should

If you have taken more Cabonni 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 Cabonni

- 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.

#### 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 Cabonni 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 reversible posterior leukoencephalopathy syndrome (RPLS). RPLS is uncommon (it affects less than 1 in 100 people).



- 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)
- Joint pain, muscle spasms
- Swollen lymph glands

#### 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 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
- 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
- Tear or hole or bleeding in your stomach or intestine, inflammation or tear of anus, bleeding in lungs or trachea (airway)
- 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 veins and the lungs
- Stroke
- 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

#### 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
- A tear or abnormal connection of the tissue in your digestive system; symptoms can include severe or persistent stomach ache
- 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
- Blood clots in the arteries
- Chest pain due to blockage in arteries, rapid heartbeat
- Liver damage, kidney failure
- Impaired hearing
- Inflammation in the eye, cataracts
- Stopping menstruation, vaginal bleeding
- A condition called posterior reversible encephalopathy syndrome (PRES) or reversible posterior leukoencephalopathy syndrome (RPLS),

which has symptoms such as seizures, headaches, confusion, or finding it difficult to concentrate

#### Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. By reporting side effects you can help provide more information on the safety of this medicine.

#### 5. How to store Cabonni

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 carton and the bottle after EXP.

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

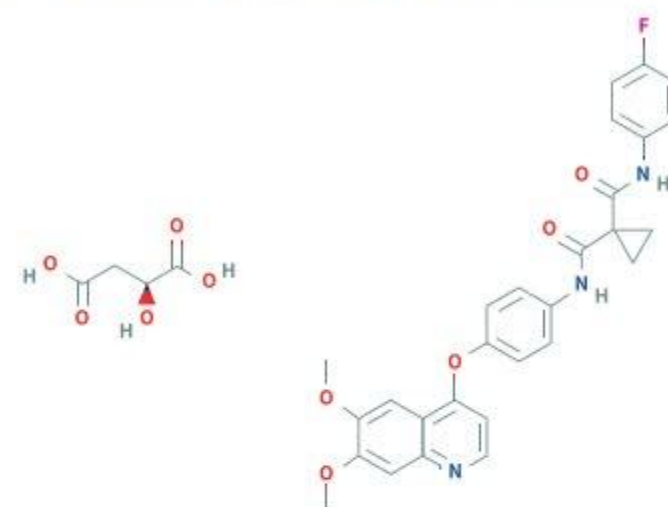
Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

#### 6. Contents of the pack and other information

##### What Cabonni contains

- The active substance is the (S)-malate salt of cabozantinib. Cabozantinib (S)-malate is described chemically as N-[4-(6,7-dimethoxyquinolin-4-yloxy)phenyl]-N''-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide,(2S)-hydroxybutane dioate. The molecular formula is C<sub>28</sub>H<sub>24</sub>FN<sub>3</sub>O<sub>5</sub>·C<sub>4</sub>H<sub>6</sub>O<sub>5</sub> and the molecular weight is 635.6 Daltons as malate salt.

The chemical structure of cabozantinib (S)-malate salt is :



- The Cabonni 20 mg capsules contain cabozantinib (S)-malate equivalent to 20 mg of cabozantinib.
- The Cabonni 80 mg 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
- Capsule shell: gelatin, iron oxide, and titanium dioxide (E171)

#### What Cabonni looks like and contents of the pack

Cabonni 20mg capsules are grey, and Cabonni 80mg capsules are orange.

Cabonni capsules are provided in blisters or in bottle, are available in cartons containing 21,28,30,56,90,112 hard capsules.

Not all pack size may be marketed.

#### Marketing Authorisation Holder

Tongmeng(Lao) Pharmaceutical and Food Co., Ltd  
Rd13 South,31km,Ban Naphasuk,Saithany District  
Vientiane  
Lao PDR

#### Manufacturer

Tongmeng(Lao) Pharmaceutical and Food Co., Ltd  
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Vientiane  
Lao PDR

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