Package leaflet: Information for the patient

CABOMETYX 20 mg film-coated tablets
CABOMETYX 40 mg film-coated tablets
CABOMETYX 60 mg film-coated tablets
cabozantinib

▼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 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 CABOMETYX is and what it is used for

What CABOMETYX is
CABOMETYX is a cancer medicine that contains the active substance cabozantinib. It is used to treat advanced stages of a type of kidney cancer called renal cell carcinoma in adults.

How CABOMETYX works
CABOMETYX 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 CABOMETYX can slow down the rate at which the tumour grows and help to cut off the blood supply that the cancer needs.

2. What you need to know before you take CABOMETYX

Do not take CABOMETYX
- 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 CABOMETYX if you:

- have high blood pressure
- 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
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- 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.

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 CABOMETYX, or stop treatment altogether. See also section 4 "*Possible side effects"*.

Children and adolescents

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

Other medicines and CABOMETYX

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 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 medicines, 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 and 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
- 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 efavirenz, ritonavir, maraviroc and emtricitabine
- Medicines used to prevent transplant rejection (ciclosporin) and ciclosporin-based regimens in rheumatoid arthritis and psoriasis

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

Taking CABOMETYX with food

You should not take CABOMETYX 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 grapefruit-

containing products for as long as you are using this medicine, as they may increase the levels of CABOMETYX in your blood.

Pregnancy, breast-feeding and fertility

Avoid becoming pregnant while being treated with CABOMETYX. 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 CABOMETYX (see also under Other medicines and CABOMETYX, above).

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

Talk to your doctor BEFORE taking CABOMETYX 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 CABOMETYX.

Women taking CABOMETYX 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 CABOMETYX may make you feel tired or weak and can affect your ability to drive or use machines.

CABOMETYX contains lactose
CABOMETYX contains lactose (a type of sugar). If you have been told by your doctor that you have an intolerance to some sugars, talk to your doctor before taking this medicine.

3. How to take CABOMETYX

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 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.

CABOMETYX should be taken once a day. The usual dose is 60 mg, however your doctor will decide on the right dose for you.

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

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

If you forget to take CABOMETYX
- 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 CABOMETYX 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 (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 stolls, bloody urine, headache, coughing up of 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 reversible posterior leukoencephalopathy syndrome (RPLS). RPLS is uncommon (it affects less than 1 in 100 people).

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
- Blisters, pain of the hands or soles of the feet, rash or redness of the skin, dry skin, skin inflammation with eruptions and flat or raised skin bumps
- Decreased appetite, weight loss, altered sense of taste
- Fatigue, weakness, headache, dizziness, , numbness, tingling, burning sensation, pain in the limbs
- Hypertension (increase in blood pressure)
- Anaemia (low levels of red blood cells)
- Reduction in platelets (which increase the risk of bleeding or bruising)
- Reduction in white blood cell count
- Redness, swelling or pain in the mouth or throat, difficulty in speaking, hoarseness, cough, dry mouth
- Changes in blood tests used to monitor general health and function of your organs (including the liver),
- Low levels of electrolytes in the blood (like magnesium, calcium, phosphate, sodium, or potassium)
- High blood potassium levels
- Increase in the level of bilirubin in your blood (which may result in jaundice/yellow skin or eyes)
- Decrease in blood level of certain type of protein (hypoalbuminaemia)
- Changes in blood tests used to monitor function of your pancreas (including increase in levels of lipase and amylase)
- Increase in blood creatinine (a chemical product of muscle activity excreted by the kidneys)
- Increase or decrease in blood sugar levels
- Increase in blood cholesterol level
- Pain in arms, legs and joints, muscle spasms
- Shortness of breath
- Protein in urine (seen in tests)

- Reduced thyroid activity; symptoms can include: tiredness, weight gain, constipation, feeling cold and dry skin
- Dehydration (lack of fluids)
- Alopecia (hair loss and thinning), hair colour change

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

- Abscess (collection of pus, with swelling and inflammation)
- Ringing in ears
- Blood clots in the lungs
- Inflammation of the pancreas
- Pain in the upper part of the abdomen
- Gastro-oesophageal reflux disease (bringing up stomach acid)
- Haemorrhoids (piles)
- Itch
- Swelling in your legs, feet, arms and hands
- Wound complications

Uncommon side effects (may affect 1 in 100 people)

- Fits
- A painful tear or abnormal connection of the tissue in your anus
- Decrease in bile flow from the liver
- Bone damage in the jaw

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.
For UK: via the Yellow Card Scheme at:www.mhra.gov.uk/yellowcard
For Ireland: via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; e-mail: medsafety@hpra.ie

By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store CABOMETYX

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, bottle label and carton after EXP. The expiry date refers to the last day of that month.

This medicinal product does not require any special storage conditions.

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

CABOMETYX 20 mg film-coated tablets: Each tablet contains cabozantinib (*S*)-malate equivalent to 20 mg of cabozantinib.
CABOMETYX 40 mg film-coated tablets: Each tablet contains cabozantinib (*S*)-malate equivalent to 40 mg of cabozantinib.
CABOMETYX 60 mg film-coated tablets: Each tablet contains cabozantinib (*S*)-malate equivalent to 60 mg of cabozantinib.

The other ingredients are:

- **Tablet contents:** microcrystalline cellulose, lactose anhydrous, hydroxypropyl cellulose, croscarmellose sodium, colloidal silicon dioxide anhydrous, magnesium stearate. (see section 2 for lactose content)
- **Film coating:** hypromellose, titanium dioxide (E171), triacetin, iron oxide yellow (E172)

What CABOMETYX looks like and contents of the pack

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 packs containing either 4 blisters with 7 tablets each (28 total), or one plastic bottle with 30 tablets.

Not all pack sizes may be marketed in your country.

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Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.