CABOMETYX®
(cabozantinib) tablets
60 mg | 40 mg | 20 mg

Take control of disease progression with CABOMETYX®[1]

CABOMETYX® is indicated as monotherapy for the treatment of adult patients with locally advanced or metastatic differentiated thyroid carcinoma (DTC), refractory or not eligible to radioactive iodine (RAI) who have progressed during or after prior systemic therapy.[1]

78%

reduction in risk of progression or death vs placebo

HR: 0.22 (96% CI: 0.15-0.32); p<0.0001[*1]

PFS

11 mo

median PFS[†]

vs 1.9 months with placebo

(96% CI: 7.4-13.8 vs 1.9-3.7, respectively)[*1]

80%

achieved disease control

vs 39% with placebo

n=130/170 vs n=34/88, respectively*‡[1]

Abridged Prescribing Information

CABOMETYX® (cabozantinib)

Presentation: Film-coated tablets containing cabozantinib (S)-malate equivalent to 20 mg, 40 mg and 60 mg cabozantinib. **Indications: CABOMETYX is indicated as monotherapy for advanced renal cell carcinoma (RCC) as first-line treatment of adult patients with intermediate or poor risk, or in adults following prior vascular endothelial growth factor (VEGF)-targeted therapy. CABOMETYX, in combination with nivolumab, is indicated for the first-line treatment of advanced renal cell carcinoma in adults. CABOMETYX is indicated as monotherapy for the treatment of hepatocellular carcinoma (HCC) in adults who have previously been treated with sorafenib**. CABOMETYX is indicated as monotherapy for the treatment of adult patients with locally advanced or metastatic differentiated thyroid carcinoma (DTC), refractory or not eligible to radioactive iodine (RAI) who have progressed during or after prior systemic therapy. **Posology & Administration**: Therapy with CABOMETYX should be initiated by a physician experienced in the administration of anticancer medicinal products. CABOMETYX as monotherapy for RCC, HCC, and DTC, the recommended dose of CABOMETYX is 60 mg once daily. CABOMETYX in combination with nivolumab in first-line advanced RCC, the recommended dose of CABOMETYX is 40 mg once daily in combination with nivolumab administered intravenously at either 240 mg every 2 weeks or 480 mg every 4 weeks. The treatment should continue until disease progression or unacceptable toxicity. Nivolumab should be continued until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression **(see the Prescribing Information (PI) for posology of Nivolumab)**. CABOMETYX therapy may be temporarily interrupted, or dose reduced to manage suspected adverse drug reactions. When dose reduction is necessary in monotherapy, it is recommended to reduce to 40 mg daily, and then to 20 mg daily. When CABOMETYX is administered in combination with nivolumab, it is recommended to reduce the dose to 20 mg of CABOMETYX once daily, and then to 20 mg every other day (refer to the Nivolumab PI for recommended treatment modification for Nivolumab). The safety and efficacy of cabozantinib in children and adolescents aged <18 years have not yet been established. **Method of Administration**: Tablets should be swallowed whole and not crushed. Patients should not eat anything for at least 2 hours before through 1 hour after taking CABOMETYX. Missed doses should not be taken if it is less than 12 hours before the next dose. **Contraindications**: Hypersensitivity to the active substance or any of the excipients. **Special warnings and precautions for use**: Monitor closely for toxicity during the first 8 weeks of treatment to determine if dose modifications are warranted. Adverse reactions that generally have early onset include hypocalcemia, hypokalemia, thrombocytopenia, hypertension, palmar-plantar erythrodysaesthesia syndrome (PPES), proteinuria, and gastrointestinal (GI) events (abdominal pain, mucosal inflammation, constipation, diarrhea, vomiting). *Hepatotoxicity*: Liver function tests should be performed before initiation and monitored closely during treatment. If liver function worsens and is considered related to CABOMETYX treatment, dose modification should be performed as per the recommended dose modification in the PI. Closer monitoring of overall safety is recommended for patients with mild or moderate hepatic impairment. A higher relative proportion of patients with moderate hepatic impairment (Child-Pugh B) developed hepatic encephalopathy with cabozantinib treatment. Cabozantinib is not recommended for use in patients with severe hepatic impairment (Child-Pugh C). *Hepatic encephalopathy*: In the HCC study (CELESTIAL), hepatic encephalopathy was reported more frequently in the cabozantinib arm than the placebo arm. Patients should be monitored for signs and symptoms of hepatic encephalopathy. *Perforations and fistulas*: Serious GI perforations and fistulas, sometimes fatal, have been observed with cabozantinib. Patients with inflammatory bowel disease, GI tumour infiltration or complications from prior GI surgery should be carefully evaluated prior to therapy and monitored closely; if GI perforation or unmanageable fistula occurs, discontinue cabozantinib. *Gastrointestinal (GI) disorders*: Diarrhoea, nausea/vomiting, decreased appetite and stomatitis/oral pain were some of the most commonly reported GI adverse reactions. Prompt medical management, including supportive care should be instituted to prevent dehydration, electrolyte imbalances and weight loss. Dose interruption/reduction or permanent discontinuation should be considered for persistent/recurrent GI adverse reactions. *Thromboembolic events*: Events of venous thromboembolism, including pulmonary embolism, and arterial thromboembolism, sometimes fatal, have been observed with cabozantinib. Cabozantinib should be used with caution in patients who are at risk for, or who have a history of, these events. Discontinue if acute myocardial infarction or any other clinically significant thromboembolic complication occurs. *Haemorrhage*: Severe haemorrhage has been observed with cabozantinib. Patients who have a history of severe bleeding prior to treatment initiation should be carefully evaluated before initiating cabozantinib therapy. Cabozantinib should not be administered to patients that have or are at risk for severe haemorrhage. *Aneurysms and artery dissections*: The use of VEGF pathway inhibitors in patients with or without hypertension may promote the formation of aneurysms and/or artery dissections. Before initiating cabozantinib, this risk should be carefully considered in patients with risk factors such as hypertension or history of aneurysm. *Thrombocytopenia*: Platelet levels should be monitored during treatment and the dose modified according to the severity of thrombocytopenia. *Wound complications*: Treatment should be stopped at least 28 days prior to scheduled surgery, including dental surgery or invasive dental procedures, if possible. Cabozantinib should be discontinued in patients with wound healing complications requiring medical intervention. *Hypertension*: Monitor blood pressure (BP); interrupt until blood pressure is controlled in case of persistent hypertension despite use of anti-hypertensives, after which Cabozantinib can be resumed at a reduced dose; discontinue if hypertension is severe and persistent despite anti-hypertensive therapy and dose reduction of cabozantinib or if hypertensive crisis occurs. *Osteonecrosis*: Osteonecrosis of the jaw (ONJ) has been observed with cabozantinib. An oral examination should be performed before initiation and periodically during treatment. Treatment should be held at least 28 days prior to scheduled dental surgery or invasive dental procedures, if possible. Use with caution in patients receiving agents associated with ONJ, such as bisphosphonates. If ONJ occurs, discontinue cabozantinib. *Palmar-plantar erythrodysaesthesia syndrome (PPES)*: Interrupt treatment if severe PPES occurs. Proteinuria: Urine protein should be monitored regularly during cabozantinib treatment. Discontinue treatment in patients who develop nephrotic syndrome. *Posterior reversible encephalopathy syndrome (PRES)*: This syndrome should be considered in any patient presenting with multiple symptoms, including seizures, headache, visual disturbances, confusion or altered mental function. Discontinue in patients with PRES. *QT interval prolongation*: Use with caution in patients with a history of QT interval prolongation, those on antiarrhythmics or with relevant pre-existing cardiac disease, bradycardia, or electrolyte disturbances. *Thyroid dysfunction*: Thyroid function tests should be performed before initiation and monitored closely during treatment. Patients with pre-existing hypothyroidism or hyperthyroidism should be treated as per standard medical practice before treatment. All patients should be observed closely for signs and symptoms of thyroid dysfunction. Patients who develop thyroid dysfunction should be treated as per standard medical practice. *Biochemical laboratory test abnormalities*: Increased incidence of electrolyte abnormalities. Hypocalcemia has been observed with cabozantinib at a higher frequency and/or increased severity (including Grade 3 and 4) in patients with thyroid cancer compared to patients with other cancers. Monitoring of biochemical parameters during treatment is recommended and appropriate replacement therapies should be used if required. *Excipients*: Do not use in patients with hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption. **Interactions**: Cabozantinib is a CYP3A4 substrate. Co-administration with strong CYP3A4 inhibitors may result in an increase in cabozantinib plasma exposure and so should be approached with caution. Co-administration with CYP3A4 inducers may result in decreased cabozantinib plasma exposure. Cabozantinib may increase the plasma concentration of P-glycoprotein substrates. MRP2 inhibitors may increase cabozantinib plasma concentrations, so concomitant use should be approached with caution. Bile salt-sequestering agents may impact absorption or reabsorption resulting in potentially decreased cabozantinib exposure. No dose adjustment is indicated when co-administered with gastric pH modifying agents. A plasma protein displacement interaction may be possible with warfarin; hence the INR values should be monitored in such combination. **Women of childbearing potential/contraception in males and females**: Ensure effective methods of contraception (oral contraceptive plus a barrier method) in male and female patients and their partners during therapy and for at least 4 months after completing the treatment. **Fertility**: Both men and women should be advised to seek advice and consider fertility preservation before treatment. **Pregnancy**: CABOMETYX should not be used during pregnancy unless the clinical condition of the woman requires treatment. **Breast-feeding**: Discontinue breast-feeding during and for at least 4 months after completing treatment. **Adverse reactions - As CABOMETYX monotherapy**: The most common serious adverse drug reactions in the RCC population (≥ 1% incidence) are, abdominal pain, diarrhoea, nausea, hypertension, embolism, hyponatraemia, pulmonary embolism, vomiting, dehydration, fatigue, asthenia, decreased appetite, deep vein thrombosis, dizziness, hypomagnesaemia and, palmar-plantar erythrodysaesthesia syndrome (PPES). The most frequent adverse reactions of any grade (experienced by at least 25% of patients) in the RCC population included diarrhoea, fatigue, nausea, decreased appetite, PPES, hypertension, weight decreased, vomiting, dysgeusia, constipation and AST increased. Hypertension was observed more frequently in the treatment naïve RCC population (67%) compared to RCC patients following prior VEGF-targeted therapy (37%). The most common serious adverse drug reactions in the HCC population (≥1% incidence) are hepatic encephalopathy, asthenia, fatigue, PPES, diarrhoea, hyponatraemia, vomiting, abdominal pain and thrombocytopenia.The most frequent adverse reactions of any grade (experienced by at least 25% of patients) in the HCC population included diarrhoea, decreased appetite, PPES, fatigue, nausea, hypertension and vomiting. The most common serious adverse drug reactions in the DTC population (≥1% incidence) are diarrhoea, pulmonary embolism, dyspnoea, deep vein thrombosis, hypertension and hypocalcaemia. The most frequent adverse reactions of any grade (experienced by at least 25% of patients) in the DTC population included diarrhoea, PPES, hypertension and fatigue. Frequency of adverse reactions based on all grades: Very common (≥*1/10*): anaemia, thrombocytopenia, hypothyroidism, decreased appetite, hypomagnesaemia, hypokalaemia, hypoalbuminaemia, dysgeusia, headache, dizziness, hypertension, haemorrhage, dysphonia, dyspnoea, cough, diarrhoea, nausea, vomiting, stomatitis, constipation, abdominal pain, dyspepsia, PPES, rash, pain in extremity, fatigue, mucosal inflammation, asthenia, peripheral oedema, weight decreased, serum ALT increased and AST increased. Common (≥*1/100 to <1/10*): abscess, neutropenia, lymphopenia, dehydration, hypophosphataemia, hyponatraemia, hypocalcaemia, hyperkalaemia, hyperbilirubinemia, hyperglycaemia, hypoglycaemia, peripheral neuropathy ,tinnitus, venous thrombosis, arterial thrombosis, pulmonary embolism, gastrointestinal perforation, pancreatitis ,fistula, gastroesophageal reflux disease, haemorrhoids, oral pain, dry mouth, dysphagia, glossodynia ,hepatic encephalopathy, pruritus, alopecia, dry skin, dermatitis acneiform, hair colour change, hyperkeratosis, erythema, muscle spasms, arthralgia, proteinuria, blood ALP increased, GGT increased, blood creatinine increased, amylase increased, lipase increased, blood cholesterol increased, and blood triglycerides increased. Uncommon (≥*1/1000 to <1/100*): convulsion, cerebrovascular accident,hepatitis cholestatic, osteonecrosis of the jaw and wound complications. Frequency not known: posterior reversible encephalopathy syndrome, myocardial infarction, aneurysms and artery dissections. **Adverse reactions - CABOMETYX in combination with nivolumab**: The most common serious adverse reactions (≥ 1% incidence) are diarrhoea, pneumonitis, pulmonary embolism, pneumonia, hyponatremia, pyrexia, adrenal insufficiency, vomiting, dehydration. The most frequent adverse reaction (≥25%) were diarrhea, fatigue, PPES, stomatitis, musculoskeletal pain, hypertension, rash, hypothyroidism, decreased appetite, nausea, and abdominal pain. Frequency of adverse reactions based on all grades: Very common (≥*1/10*): upper respiratory tract infection, hypothyroidism, hyperthyroidism, decreased appetite, dysgeusia, dizziness, headache, hypertension, dysphonia, dyspnoea, cough, diarrhoea, vomiting, nausea, constipation, stomatitis, abdominal pain, dyspepsia, PPES, rash, pruritus, musculoskeletal pain, arthralgia, muscle spasm, proteinuria, fatigue, pyrexia, oedema, increased ALT, increased AST, hypophosphataemia, hypocalcaemia, hypomagnesaemia, hyponatraemia, hyperglycaemia, lymphopenia, increased alkaline phosphatase, increased lipase, increased amylase, thrombocytopenia, increased creatinine, anaemia, leucopoenia, hyperkalaemia, neutropaenia,hypercalcaemia, hypoglycaemia, hypokalaemia, increased total bilirubin, hypermagnesaemia,hypernatraemia, weight decreased. Common (≥*1/100 to <1/10*): pneumonia, eosinophilia, hypersensitivity (including anaphylactic reaction), adrenal insufficiency, dehydration, peripheral neuropathy, tinnitus, dry eye, blurred vision, atrial fibrillation, tachycardia, thrombosis, pneumonitis, pulmonary embolism, epistaxis, pleural effusion, colitis, gastritis, oral pain, dry mouth, haemorrhoids, hepatitis, alopecia, dry skin, erythema, hair colour change, arthritis, renal failure, acute kidney injury, pain, chest pain, blood cholesterol increased, hypertriglyceridaemia. Uncommon (≥*1/1000 to <1/100*): infusion related hypersensitivity reaction, hypophysitis, thyroiditis, encephalitis autoimmune, Guillain-Barré syndrome, myasthenic syndrome, uveitis, myocarditis, pancreatitis, small intestine perforation, glossodynia, psoriasis, urticaria, myopathy, osteonecrosis of the jaw, fistula, nephritis.

Reference: Cabometyx® Malaysia Prescribing Information (Date of Revision August 2022).

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Full prescribing information is available upon request, please refer to full prescribing information before prescribing.
For adverse events reporting, please report to ZPMYPV@zuelligpharma.com

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Innovation for patient care

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