PRESCRIBING INFORMATION

CABOMETYX® ▼ (cabozantinib)

Presentation: Film-coated unscored tablets containing cabozantinib (S)-malate equivalent to 20mg, 40mg and 60mg cabozantinib. **Indications:** treatment of advanced renal cell carcinoma (RCC) in adults following prior vascular endothelial growth factor (VEGF)-targeted therapy. **Dosage:** See Summary of Product Characteristics (SPC) for full information. Therapy with CABOMETYX should be initiated by a physician experienced in the administration of anticancer medicinal products. **Cabozantinib presentations are not bioequivalent and should not be used interchangeably. Please refer to the SPCs for further information.** Recommended dose is 60mg orally once daily, at least 2 hours after and 1 hour before food. Continue until no further clinical benefit or unacceptable toxicity. CABOMETYX therapy may be temporarily interrupted or dose reduced to manage suspected adverse reactions. The safety and efficacy of cabozantinib in children and adolescents aged <18 years has not yet been established. Do not crush the tablets, and swallow whole. See SPC for dosing in special populations and modifications for adverse reactions. **Contraindications:** Hypersensitivity to the active substance or any of the excipients. **Special warnings and precautions:** Monitor closely for toxicity during first 8 weeks of therapy. Events that generally have early onset include hypocalcaemia, hypokalaemia, thrombocytopenia, hypertension, palmar-plantar erythrodysaesthesia syndrome (PPES), proteinuria, and gastrointestinal (GI) events. *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 evaluated prior to therapy and monitored; if perforation and unmanageable fistula occur, discontinue cabozantinib. *Thromboembolic events*: use with caution in patients with a history of or risk factors for thromboembolism; discontinue if acute myocardial infarction (MI) or other significant arterial thromboembolic complication occurs. *Haemorrhage*: not recommended for patients that have or are at risk of severe haemorrhage. *Wound complications*: treatment should be stopped at least 28 days prior to scheduled surgery (including dental). *Hypertension*: monitor blood pressure (BP); reduce with persistent hypertension and discontinue should uncontrolled hypertension or hypertensive crisis occur. *PPES*: interrupt treatment if severe PPES occurs. *Proteinuria*: discontinue in patients with nephrotic syndrome. *Reversible posterior leukoencephalopathy syndrome (RPLS)*: discontinue in patients with RPLS. *QT prolongation*: use with caution in patients with a history of QT prolongation, those on antiarrythmics or with pre-existing cardiac disease. *Excipients:* do not use in patients with hereditary problems of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption. **Interactions:** Cabozantinib is a CYP3A4 substrate. Potent CYP3A4 inhibitors may result in an increase in cabozantinib plasma exposure (e.g. ritonavir, itraconazole, erythromycin, clarithromycin, grapefruit juice). Coadministration with CYP3A4 inducers may result in decreased cabozantinib plasma exposure (e.g. rifampicin, phenytoin, carbamazepine, phenobarbital, St John's Wort). Cabozantinib may increase the plasma concentration of P-glycoprotein substrates (e.g. fexofenadine, aliskiren, ambrisentan, dabigatran etexilate, digoxin, colchicine, maraviroc, posaconazole, ranolazine, saxagliptin, sitagliptin, talinolol, tolvaptan). MRP2 inhibitors may increase cabozantinib plasma concentrations (e.g. cyclosporine, efavirenz, emtricitabine). Bile salt sequestering agents may impact absorption or reabsorption resulting in potentially decreased cabozantinib exposure. No dose adjustment when coadministered with gastric pH modifying agents.

A plasma protein displacement interaction may be possible with warfarin. INR values should be monitored in such a combination. **Women of childbearing potential/contraception in males and females:** Ensure effective measures 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 treatment. **Pregnancy:** CABOMETYX should not be used during pregnancy unless the clinical condition of the woman requires treatment. *Lactation* – discontinue breast-feeding during and for at least 4 months after completing treatment. **Adverse reactions:** The most common serious adverse reactions are abdominal pain (3%), pleural effusion (3%), diarrhoea (2%) and nausea (2%). *Very common (≥1/10)*: anaemia, hypothyroidism, decreased appetite, hypophosphataemia, hypoalbuminaemia, hypomagnesaemia, hyponatraemia, hypokalaemia, hyperkalaemia, hypocalcaemia, hyperbilirubinaemia, dysgeusia, headache, dizziness, hypertension, dysphonia, dyspnoea, cough, diarrhoea, nausea, vomiting, stomatitis, constipation, abdominal pain, dyspepsia, PPES, rash, dry skin, pain in extremity, muscle spasms, arthralgia, proteinuria, fatigue, mucosal inflammation, asthenia, weight decreased, serum ALT, AST and ALP increased, creatinine increased, triglycerides increased, hyperglycaemia, hypoglycaemia, lymphopenia, neutropenia, thrombocytopenia, GGT increased, amylase increased, blood cholesterol increased, lipase increased. *Common (≥1/100 to <1/10)*: abscess, dehydration, tinnitus, pulmonary embolism, upper abdominal pain, gastrooesophageal reflux disease, haemorrhoids, pruritus, alopecia, peripheral oedema. *Uncommon (≥1/1000 to <1/100):* convulsion, anal fistula, pancreatitis, hepatitis cholestatic, osteonecrosis of the jaw. *Selected adverse events:* GI perforation, fistula, haemorrhage, RPLS. Prescribers should consult the SPC in relation to other adverse reactions. **Legal category:** POM. **Basic NHS cost:** £5143 per bottle **Package quantity:** Bottles containing 30 tablets. **Marketing authorisation numbers:** EU/1/16/1136/001-006. **Marketing authorisation holder:** Ipsen Pharma, 65 quai Georges Gorse, 92100 Boulogne-Billancourt, France. Further information can be obtained from IPSEN Ltd, 190 Bath Road, Slough, Berkshire, SL1 3XE. Tel: 01753 627777. CABOMETYX® is a registered trademark. **Date of preparation of PI**: November 2017. **CMX-GB-000058**

Adverse events should be reported.
Reporting forms and information can be found at www.mhra.gov.uk/yellowcard
Adverse events should also be reported to the Ipsen Medical Information department on 01753 627777 or medical.information.uk@ipsen.com