CABOZANTINIB (Cabometyx)

INDICATION (ICD10) C22, C64

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (CAB02) (CAB03) (CAB04)

1. The treatment of previously treated metastatic or inoperable locally advanced **renal cell** carcinoma with a clear cell component. Previously received at least 1 vascular endothelial growth factor (VEGF)-targeted systemic therapy or has received prior treatment with an anti-PD-1, anti-PD-L1, anti-PD-L2, anti-CD137, or anti-Cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) antibody for renal cancer and has not been previously treated with cabozantinib and has progressed on previous treatment or within 6 months of most recent dose of VEGF inhibitor. If has brain metastases then these have been treated and are stable. PS 0 or 1. (TA463)
2. The treatment of treatment-naïve to vascular endothelial growth factor (VEGF)-targeted therapy metastatic or inoperable locally advanced intermediate or poor risk advanced **renal cell** carcinoma with a clear cell component. If has brain metastases then these have been treated and are stable. PS 0, 1 or 2. (TA542)
3. Cabozantinib monotherapy for the second line of tyrosine kinase inhibitor systemic therapy of Child-Pugh A locally advanced or metastatic **hepatocellular** carcinoma previously treated with sorafenib. PS 0 or 1. (TA849)

REGIMEN

CABOZANTINIB 60mg orally daily

CYCLE FREQUENCY AND NUMBER OF CYCLES

Daily continuously as long as clinical benefit or toxicity.
A formal medical review as to whether treatment with cabozantinib should continue or not will be scheduled to occur at least by the end of the first 8 weeks of treatment.

ADMINISTRATION

Available as 20mg, 40mg and 60mg tablets
Swallow whole. Not to eat anything for at least 2 hours before until 1 hour after taking cabozantinib
Grapefruit and grapefruit juice should be avoided while on cabozantinib.

ANTI-EMETICS

Minimal risk all days

CONCURRENT MEDICATION REQUIRED

Cabozantinib	Loperamide

EXTRAVASATION AND TYPE OF LINE / FILTERS

Not applicable

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E and LFTs minimum monthly
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
Thyroid function tests baseline, then every 3 months
Blood pressure weekly for cycle 1 then every month

MAIN TOXICITES AND ADVERSE REACTIONS

Cabozantinib	Diarrhoea Hand-foot syndrome Haemorrhage Hypertension Hypothyroidism Proteinurea Wound healing delayed

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS
(not exhaustive list check SPC/BNF/Stockleys)

Cabozantinib	Lots of interactions, causing bleeding, QT prolongation and hypokalaemia etc. Check interactions carefully.

DOSE MODIFICATIONS

Cabozantinib dose

Recommended dose	60mg daily
First dose adjustment	40mg daily
Second dose adjustment	20mg daily

Grade 1 and grade 2 adverse reactions which are tolerable and easily managed	Dose adjustment is usually not required. Add supportive care as indicated.
Grade 2 adverse reactions which are intolerable and cannot be managed with a dose reduction or supportive care	Interrupt treatment until the adverse reaction resolves to grade ≤1. Add supportive care as indicated. Consider re-initiating at a reduced dose.
Grade 3 adverse reactions	Interrupt treatment until the adverse reaction resolves to grade ≤1. Add supportive care as indicated. Re-initiate at a reduced dose.
Grade 4 adverse reactions	Interrupt treatment. Institute appropriate medical care. If adverse reaction resolves to grade ≤1, re-initiate at a reduced dose. If adverse reaction does not resolve, permanently discontinue

Non-haematogical

Cabozantinib

Haemorrhage	Severe haemorrhage, sometimes fatal, 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.
Hypertension	Blood pressure should be well-controlled prior to initiating cabozantinib. During treatment with cabozantinib, all patients should be monitored for hypertension and treated as needed with standard anti-hypertensive therapy. In the case of persistent hypertension despite use of anti-hypertensives, the cabozantinib dose should be reduced. Cabozantinib should be discontinued if hypertension is severe and persistent despite anti-hypertensive therapy and dose reduction of cabozantinib. In case of hypertensive crisis, cabozantinib should be discontinued.
Palmar plantar	When PPES is severe, interruption of treatment with cabozantinib should be considered. Cabozantinib should be restarted with a lower dose when PPES has been resolved to grade 1.
Perforations and fistulas	Cabozantinib should be discontinued in patients who experience a GI perforation or a fistula that cannot be adequately managed.
Posterior reversible encephalopathy syndrome	Cabozantinib treatment should be discontinued in patients with PRES.
Proteinuria	Proteinuria has been observed with cabozantinib. Urine protein should be monitored regularly during cabozantinib treatment. Cabozantinib should be discontinued in patients who develop nephrotic syndrome.
Thrombocytopenia	Platelet levels should be monitored during cabozantinib treatment and the dose modified according to the severity of the thrombocytopenia
Thromboembolic events	Cabozantinib should be discontinued in patients who develop an acute myocardial infarction or any other clinically significant thromboembolic complication.
Wound healing and osteonecrosis	Cabozantinib treatment should be stopped at least 28 days prior to scheduled surgery, including dental surgery or invasive dental procedures, if possible. The decision to resume cabozantinib therapy after surgery should be based on clinical judgment of adequate wound healing. Cabozantinib should be discontinued in patients with wound healing complications requiring medical intervention. Cabozantinib treatment should be held at least 28 days prior to scheduled dental surgery or invasive dental procedures, if possible. Caution should be used in patients receiving agents associated with ONJ, such as bisphosphonates. Cabozantinib should be discontinued in patients who experience ONJ.

Hepatic impairment

Cabozantinib

Child-Pugh scores are based on ascites, encephalopathy, INR, albumin, total bilirubin

Severe hepatic impairment (Child-Pugh C).	Not recommended

Renal impairment

Cabozantinib

Cabozantinib should be used with caution in patients with mild or moderate renal impairment (CrCl 30–59ml/min). Cabozantinib is not recommended for use in patients with CrCl<30ml/min.

REFERENCES

1. Choueiri et al, Lancet Oncology June 2016, 17 (7): 917-927