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/)

The treatment of previously treated advanced renal cell carcinoma where the following criteria are met:

2. Histological diagnosis of renal cell carcinoma with a clear cell component. Note papillary, chromophobe and Xp11 translocation sub types can be treated as per clear cell pathway
3. Either metastatic disease or inoperable locally advanced disease
4. 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.
5. Progressed on previous treatment or within 6 months of most recent dose of VEGF inhibitor
6. Performance status of 0 or 1
7. If the patient has brain metastases then these have been treated and are stable
8. Cabozantinib is to be continued until disease progression or unacceptable toxicity or the patient's choice to stop treatment
9. 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
10. No planned treatment breaks of more than 6 weeks beyond the expected cycle length are allowed (to allow any toxicity of current therapy to settle or intercurrent comorbidities to improve).**Requests for continuation of treatment after unplanned treatment breaks over this duration should be made via the treatment break approval process.
11. Cabozantinib will otherwise be used as set out in its Summary of Product Characteristics

The treatment of treatment-naïve intermediate or poor risk advanced renal cell carcinoma where the following criteria are met:

2. This patient has a confirmed histological diagnosis of renal cell carcinoma (RCC) with a clear cell component. Note papillary, chromophobe and Xp11 translocation sub types can be treated as per clear cell pathway
3. The patient has either metastatic disease or inoperable locally advanced disease
4. The patient is treatment naïve to systemic therapy and in particular has previously received neither any vascular endothelial growth factor (VEGF)-targeted systemic therapy nor mTOR pathway inhibitor-targeted treatment unless prior treatment with pazopanib or sunitinib or tivozanib has had to be stopped solely as a consequence of dose-limiting toxicity and in the clear absence of progressive disease
5. The patient has intermediate risk OR poor risk advanced renal cell carcinoma as defined by the International Metastatic Renal Cell Carcinoma
Database Consortium. Good risk patients are not eligible for cabozantinib therapy.
Intermediate risk is defined as having 1 or 2 risk factors and poor risk as having ≥3 factors, these factors being:
- Time from diagnosis of RCC to need for systemic therapy of <1 year
- Haemoglobin < lower limit of normal
- Corrected calcium > upper limit of normal
- Karnofsky performance status <80%
- Neutrophils > upper limit of normal
- Platelet count > upper limit of normal

6. The patient has an ECOG performance status of either 0 or 1 or 2
7. If the patient has brain metastases, then these have been treated and are stable

8. Cabozantinib is to be continued until loss of clinical benefit or unacceptable toxicity or patient choice to stop treatment
9. 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
10. No treatment breaks of more than 6 weeks beyond the expected cycle length are allowed (to allow any toxicity of current therapy to settle or
intercurrent comorbidities to improve)*
*Requests for continuation of treatment after unplanned treatment breaks over this duration should be made via the treatment break approval process.
11. Cabozantinib is to be otherwise used as set out in its Summary of Product Characteristics.

Cabozantinib for the second line of tyrosine kinase inhibitor systemic therapy of Child-Pugh A locally advanced or metastatic hepatocellular carcinoma previously treated with sorafenib
2. Has been previously treated with sorafenib for locally advanced or metastatic hepatocellular carcinoma.
3. Currently has Child-Pugh liver function class A.
Note: NICE has not recommended cabozantinib for patients with Child-Pugh liver function class B.
4. ECOG performance status of 0 or 1. Note: NICE has not recommended cabozantinib in patients with an ECOG performance status of 2 or more.
5. The only other TKI with which the patient has been previously treated is sorafenib unless regorafenib has had to be stopped within 3 months of its start solely as a consequence of dose-limiting toxicity and in the clear absence of disease progression.
6. Has not been previously treated with cabozantinib.
7. Cabozantinib is to be used only as monotherapy.
8. Cabozantinib is to be continued until loss of clinical benefit or unacceptable toxicity or patient choice to stop treatment, whichever is the sooner.
9. A formal medical review as to whether treatment with cabozantinib should continue or not will be scheduled to occur no later than by the end of the 2nd month of therapy.
10. When a treatment break of more than 6 weeks beyond the expected 4-weekly cycle length is needed, I will complete a treatment break form to restart treatment, including an indication as appropriate if the patient had an extended break because of COVID 19.
11. Cabozantinib will be otherwise used as set out in its Summary of Product Characteristics.

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