Cabozantanib –alternate schedule (Unlicensed)

Indication

Treatment of advanced renal cell carcinoma (RCC):
· In treatment-naïve adults with intermediate or poor risk
· In adults following prior vascular endothelial growth factor (VEGF)-targeted therapy
Used in patients with toxicity on daily schedule

Regimen details

Table 1 – Treatment regimen details

DRUG	DOSE	ROUTE	FREQUENCY/DURATION
Cabozantanib	60mg	po	Once daily Days 1-14 & Days 22-35

Cycle frequency

6 weeks

Number of cycles

Treatment should continue for as long as clinical benefit is observed or unacceptable toxicity occurs

Administration

Oral
Tablets should be swallowed whole and not crushed, patients should not eat anything for at least 2 hours before and 1 hours after
If the patient misses a dose, the missed dose should not be taken if it is less than 12 hours before the next dose

Pre-medication

N/A

Emetogenicity – consult anti-emetic policy for full details

Minimum Risk (Category D)

Additional supportive medication

N/A

Investigations – pre first cycle

Table 2 - Standard Investigations prior to first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
LFT (including AST)	14 days
CT Scan	28 days
Baseline ECG	28days
Blood Pressure	14 days

Investigations –pre subsequent cycles

FBC, U+E (including creatinine), LFT (including AST), Blood Pressure

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant.

Table 3 – Standard test result limits for each administration to go ahead

Investigation	Limit
Neutrophil count	≥ 1.0 x 10^9/L
Platelet count	≥ 100 x 10^9/L
WCC	≥2 x 10 9/L
AST	< 3 x ULN
Hb	≥ 8g/dL
Creatinine	< 200µmol/l
Bilirubin	≤ 1.5 x ULN
Corrected QT Interval	< 480 milliseconds

Dose modifications

Dose interruptions are recommended for management of CTCAE grade 3 or greater toxicities or intolerable grade 2 toxicities

Dose reductions are recommended for events that, if persistent, could become serious or intolerable

If required, doses should be reduced to 40mg daily then 20mg daily.

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

The most common serious adverse reactions associated with cabozantinib are:

- Pneumonia
- mucosal inflammation
- hypocalcaemia
- dysphagia
- dehydration
- pulmonary embolism
- hypertension

- **Frequently occurring side effects**

The most frequent adverse reactions of any grade (experienced by at least 20% of patients) included:

- diarrhoea
- PPES
- weight decreased
- decreased appetite
- nausea
- fatigue
- dysgeusia
- hair colour changes
- hypertension
- stomatitis
- constipation
- vomiting
- mucosal inflammation
- asthenia
- dysphonia

- **Other side effects**

The most common laboratory abnormalities were:

- increased aspartate aminotransferase (AST)
- increased alanine aminotransferase (ALT)
- increased alkaline phosphatase (ALP)
- lymphopenia
- hypocalcaemia
- neutropenia
- thrombocytopenia
- hypophosphataemia
- hyperbilirubinemia
- hypomagnesaemia
- hypokalaemia

Significant drug interactions – for full details consult product literature/ reference texts

Effect of other medicinal products on cabozantinib

CYP3A4 inhibitors and inducers:

Strong CYP3A4 **inhibitors** (e.g., ritonavir, itraconazole, erythromycin, clarithromycin, grapefruit juice) my decrease cabozantinib clearance and increase plasma cabozantinib exposure. Use with caution.

Strong CYP3A4 **inducers** (e.g., phenytoin, carbamazepine, rifampicin, phenobarbital or herbal preparations containing St. John's Wort [Hypericum perforatum]) significantly increases clearance of cabozantinib and decreases plasma cabozantinib exposure. Concurrent use should therefore be avoided.

MRP2 inhibitors:

In vitro data demonstrate that cabozantinib is a substrate of MRP2. Therefore, administration of MRP2 inhibitors may result in increases in cabozantinib plasma concentrations.

Effect of cabozantinib on other medicinal products

The effect of cabozantinib on the pharmacokinetics of contraceptive steroids has not been investigated. As unchanged contraceptive effect may not be guaranteed, an additional contraceptive method, such as a barrier method, is recommended.

An interaction with warfarin may be possible. In case of such combination, INR values should be monitored.

P-glycoprotein substrates:

Cabozantinib may have the potential to increase plasma concentrations of P-gp substrate (e.g., fexofenadine, aliskiren, ambrisentan, dabigatran etexilate, digoxin, colchicine, maraviroc, posaconazole, ranolazine, saxagliptin, sitagliptin, talinolol, tolvaptan). co-administered substrates of P-gp. Subjects should be cautioned regarding taking while receiving cabozantinib.

Additional comments

References

1. Cabozantinib SPC Updated 10/05/2022
2. NICE TA 463 – August 2017
3. NICE TA 542 – October 2018