A - Regimen Name

**CABO Regimen**

Cabozantinib (Tablet)

**Disease Site**  
Genitourinary - Renal Cell / Kidney

**Intent**  
Palliative

**Regimen Category**  
Evidence-Informed:

Regimen is considered appropriate as part of the standard care of patients; meaningfully improves outcomes (survival, quality of life), tolerability or costs compared to alternatives (recommended by the Disease Site Team and national consensus body e.g. pan-Canadian Oncology Drug Review, pCODR). Recommendation is based on an appropriately conducted phase III clinical trial relevant to the Canadian context OR (where phase III trials are not feasible) an appropriately sized phase II trial. Regimens where one or more drugs are not approved by Health Canada for any indication will be identified under Rationale and Use.

**Rationale and Uses**  
For the treatment of adult patients with advanced or metastatic renal cell carcinoma (RCC) that had progressed after prior vascular endothelial growth factor (VEGF)-targeted therapy.
B - Drug Regimen

**cabozantinib (tablet)** 60 mg PO Daily

(This drug is not currently publicly funded for this regimen and intent)

Cabozantinib tablets and capsules are **not interchangeable**.

C - Cycle Frequency

**CONTINUOUS TREATMENT**

Until disease progression or unacceptable toxicity

D - Premedication and Supportive Measures

**Antiemetic Regimen:** Low – No routine prophylaxis; PRN recommended

**Other Supportive Care:**
Also refer to [CCO Antiemetic Recommendations](#).

E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated.

Prior to initiating cabozantinib therapy:

- Blood pressure should be well-controlled.
- Hypokalemia, hypomagnesemia, and hypocalcemia should be corrected.
- Optimal control of thyroid function is recommended.

Hold treatment for at least 28 days prior to scheduled surgery, including dental surgery; resume based on clinical judgment of adequate wound healing.
**Dosage with toxicity**

**Dose Levels**

<table>
<thead>
<tr>
<th>Dose Level</th>
<th>Cabozantinib (Tablet) Dose (mg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>60</td>
</tr>
<tr>
<td>-1</td>
<td>40</td>
</tr>
<tr>
<td>-2*</td>
<td>20</td>
</tr>
<tr>
<td>-3</td>
<td>Discontinue</td>
</tr>
</tbody>
</table>

*If previously receiving 20 mg daily, restart at 20 mg if tolerated. Otherwise, discontinue.

**Toxicity**

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Severity</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Related hematologic/ non-hematologic/ organ toxicity</td>
<td>Intolerable grade 2 and cannot be adequately managed</td>
<td>Hold*; consider restart at 1 dose level ↓</td>
</tr>
<tr>
<td></td>
<td>Grade 3</td>
<td>Hold*; restart at 1 dose level ↓</td>
</tr>
<tr>
<td></td>
<td>Grade 4</td>
<td>Hold*; restart at 1 dose level ↓ or Discontinue</td>
</tr>
<tr>
<td>Unmanageable fistula or GI perforation</td>
<td>Any</td>
<td>Discontinue</td>
</tr>
<tr>
<td>Severe hemorrhage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arterial thromboembolic event (e.g. MI, cerebral infarction)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Torsade de pointes or polymorphic ventricular tachycardia or signs/symptoms of serious arrhythmia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertensive crisis, severe uncontrolled hypertension despite optimal therapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nephrotic syndrome</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Reversible posterior leukoencephalopathy syndrome (or PRES)

Wound healing complications requiring medical intervention

*Restart if toxicity resolved to ≤ grade 1 or baseline. Discontinue if toxicity does not resolve after 6 weeks.

### Hepatic Impairment

<table>
<thead>
<tr>
<th>Liver Impairment</th>
<th>Cabozantinib (Tablet) Starting Dose (mg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild or moderate (Child-Pugh classes A and B)</td>
<td>40 mg</td>
</tr>
<tr>
<td>Severe (Child-Pugh class C)</td>
<td>Not recommended (has not been studied)</td>
</tr>
</tbody>
</table>

### Renal Impairment

<table>
<thead>
<tr>
<th>Renal Impairment</th>
<th>Cabozantinib (Tablet) Dose (mg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild or moderate (eGFR ≥ 30mL/min)</td>
<td>No dosage adjustment required</td>
</tr>
<tr>
<td>Severe (eGFR &lt;29 mL/min)</td>
<td>Not recommended (has not been studied)</td>
</tr>
</tbody>
</table>

### Dosage in the Elderly

No dosage adjustment is required. There were no overall differences in safety or efficacy between patients aged 65 or older and younger patients.
Dosage based on Ethnicity:

There were no overall differences in PK based on race.

F - Adverse Effects

Refer to cabozantinib (tablet) drug monograph(s) for additional details of adverse effects

<table>
<thead>
<tr>
<th>Very common (≥ 50%)</th>
<th>Common (25-49%)</th>
<th>Less common (10-24%)</th>
<th>Uncommon (&lt; 10%), but may be severe or life-threatening</th>
</tr>
</thead>
<tbody>
<tr>
<td>▲ LFTs (may be severe)</td>
<td>Abnormal electrolyte(s)</td>
<td>Dysgeusia</td>
<td>Arterial / venous thromboembolism</td>
</tr>
<tr>
<td>Diarrhea (may be severe)</td>
<td>Anorexia, weight loss</td>
<td>Abdominal pain</td>
<td>QT prolongation</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Palmar-plantar erythrodysesthesi syndrome (PPES)</td>
<td>Rash / dry skin</td>
<td>Hemorrhage</td>
</tr>
<tr>
<td>Nausea, vomiting</td>
<td>Hypertension (may be severe)</td>
<td>Mucositis</td>
<td>Wound complication</td>
</tr>
<tr>
<td></td>
<td>▼ albumin</td>
<td>Hypothyroidism</td>
<td>Gastrointestinal GI fistula</td>
</tr>
<tr>
<td></td>
<td>Myelosuppression</td>
<td>Dysphonia</td>
<td>GI perforation</td>
</tr>
<tr>
<td></td>
<td>Constipation</td>
<td>Cough, dyspnea</td>
<td>Cholestasis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Musculoskeletal pain</td>
<td>Pancreatitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dyspepsia</td>
<td>Osteonecrosis of jaw</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Proteinuria</td>
<td>Reversible Posterior Leukoencephalopathy Syndrome (RPLS)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dizziness</td>
<td>Syncope</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Headache</td>
<td>Pleural effusion</td>
</tr>
</tbody>
</table>

G - Interactions

Refer to cabozantinib (tablet) drug monograph(s) for additional details
Cabozantinib is primarily metabolized by CYP3A4 and is susceptible to inhibitors and inducers of this isoenzyme. Avoid co-administration with strong CYP3A4 inducers and consider alternatives to strong CYP3A4 inhibitors.

- Avoid co-administration to the extent possible with QTc interval-prolonging drugs.

H - Drug Administration and Special Precautions

Refer to cabozantinib (tablet) drug monograph(s) for additional details

Administration

- Oral self-administration; drug available by outpatient prescription.
- Tablets should be swallowed whole, not chewed or crushed.
- Tablets should be administered on an empty stomach (no food for at least 2 hours before and 1 hour after taking a dose).
- Avoid grapefruit, starfruit, Seville oranges, their juices or products during treatment.
- If a dose is missed, additional dose should not be taken within 12 hours of the next dose.
- Cabozantinib should be stored between 15°C to 25°C

Contraindications

- Patients who have a hypersensitivity to this drug or any of its components

Other Warnings/Precautions:

- Patients with a history of severe bleeding should be evaluated carefully before starting treatment. Do not give cabozantinib to patients with or at risk for severe hemorrhage.
- Use cabozantinib with caution in patients at risk for, or who have a history of:
  - venous and/or arterial thromboembolism
  - hypertension
  - inflammatory bowel disease, tumour infiltration in the GI tract, or complications from prior GI surgery (particularly when associated with delayed or incomplete healing)
- severe bleeding
- low heart rate at baseline (< 60 beats per minute).
- Syncope/arrhythmia, QT prolongation, sick sinus syndrome, sinoatrial block, atrioventricular (AV) block, ischemic heart disease, or congestive heart failure.

- Use caution when driving or operating machinery as cabozantinib may cause fatigues, dizziness and weakness.

Pregnancy and lactation:

- Cabozantinib is not recommended for use in pregnancy. At least 2 forms of adequate contraception (i.e. oral contraceptives and barrier method) should be used by both sexes during treatment, and for at least 4 months after the last dose.
- Breastfeeding is not recommended during treatment and for 4 months after the last dose.
- Fertility effects: Probably. Documented in animals

I - Recommended Clinical Monitoring

Recommended Clinical Monitoring

- ECG, heart rate and blood pressure; Baseline and as clinically indicated
- Electrolytes, including calcium, potassium and magnesium; Baseline and as clinically indicated, especially in patients at risk of severe arrhythmias
- Liver function tests; Baseline and as clinically indicated
- Renal function tests; Baseline and as clinically indicated
- Thyroid function tests; Baseline and as clinically indicated
- Clinical toxicity assessment for GI effects (including perforations, fistulas), bleeding, skin effects including PPES, respiratory and neurologic effects, thromboembolism, proteinuria, pancreatitis, osteonecrosis of the jaw and wound healing complications; At each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for
Suggested Clinical Monitoring

- Blood glucose and lipid profile; Baseline and as clinically indicated
- INR for patients receiving warfarin; Baseline and as clinically indicated

K - References

Cabozantinib drug monograph, Cancer Care Ontario.


M - Disclaimer

Regimen Abstracts

A Regimen Abstract is an abbreviated version of a Regimen Monograph and contains only top level information on usage, dosing, schedule, cycle length and special notes (if available). It is intended for healthcare providers and is to be used for informational purposes only. It is not intended to constitute or be a substitute for medical advice, and all uses of the Regimen Abstract are subject to clinical judgment. Such information is provided on an “as-is” basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information’s quality, accuracy, currency, completeness, or reliability, and Cancer Care Ontario disclaims all liability for the use of this information, and for any claims, actions, demands or suits that arise from such use.

Information in regimen abstracts is accurate to the extent of the ST-QBP regimen master listings, and has not undergone the full review process of a regimen monograph. Full regimen monographs will be published for each ST-QBP regimen as they are developed.

Regimen Monographs

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.
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