**Regimen Monograph**

Regimen Name | Drug Regimen | Cycle Frequency | Premedication and Supportive Measures | Dose Modifications | Adverse Effects | Interactions | Drug Administration and Special Precautions | Recommended Clinical Monitoring | Administrative Information | References | Other Notes | Disclaimer

## A - Regimen Name

# SUNI Regimen
**SUNItinib**

**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** Treatment of metastatic renal cell carcinoma of clear cell histology:

- First-line therapy in patients with good or intermediate risk factor
- Second-line therapy for patients who have documented failure to first-line cytokine based therapy

**Supplementary Public Funding** **SUNItinib**
Exceptional Access Program (SUNItinib - Metastatic renal cell carcinoma, with specific criteria) (EAP Website)

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## B - Drug Regimen

| | | | |
|---|---|---|---|
| **SUNItinib** | 50 mg | PO | daily, days 1 to 28, every 6 weeks |

(Outpatient prescription in multiples of 12.5mg, 25mg and 50mg capsules)

**Alternative schedule:**

| | | | |
|---|---|---|---|
| **SUNItinib** | 50 mg | PO | daily, days 1 to 14 every 3 weeks |

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## C - Cycle Frequency

**Standard schedule: REPEAT EVERY 6 WEEKS (4 WEEKS ON, 2 WEEKS OFF)**

**Alternative schedule: REPEAT EVERY 3 WEEKS (2 WEEKS ON, 1 WEEK OFF)**

Until disease progression or unacceptable toxicity.

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## D - Premedication and Supportive Measures

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

**Other Supportive Care:**

Also refer to CCO Antiemetic Recommendations.

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## E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated. The following recommendations have been adapted from clinical trials or product monographs and could be considered.

Sunitinib may be given with or without food. Daily doses should not exceed 50mg nor be decreased below 25mg. Doses should be held prior to surgery

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Suggested dose levels are 50 mg, 37.5 mg and 25 mg. Doses reduced for toxicity should not be re-escalated.

**Dosage with toxicity**

| Toxicity | Action | Dose |
|---|---|---|
| Severe hypertension | Hold and treat appropriately. | May resume only if hypertension is controlled.<br><br>(See Appendix 8: Management of Angiogenesis Inhibitor (AI) Induced Hypertension) |
| CHF, arrhythmia, ↑ QTc, AV block, pancreatitis, hepatic failure, nephrotic syndrome, RPLS, perforation, fistula, TMA, ITP, TTP, HUS, DIC, hemolysis, Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme*, necrotizing fasciitis | Discontinue | Not applicable |
| Asymptomatic falls in LVEF < LLN or ≥ 20% ↓ from baseline, thrombotic microangiopathy, grade 3 hemorrhage | Hold until ≤ Grade 1 | ↓ 1 dose level |
| Other grade 3 non-hematological toxicity, including ↑ LFTs | Hold until ≤ Grade 2 | ↓ 1 dose level |
| Grade 3 or 4 hematological (excluding lymphopenia) | Hold until ≤ Grade 2 | ↓ 1 dose level |
| Grade 4 non-hematological toxicity, including ↑ LFTs | Discontinue | Not applicable |

* may consider rechallenge at a lower dose after resolution of erythema multiforme if clinically indicated.

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## Hepatic Impairment

Multiple dosing pharmacokinetic studies have not been conducted; single dose studies have only been conducted in patients with mild-moderate hepatic impairment, Hepatic metabolism / excretion is significant; consider dose modification for patients with mild to moderate impairment (Child Pugh A and B).

## Renal Impairment

Only single dose studies have been conducted in patients with renal impairment. No adjustment to starting dose is required in patients with mild to severe renal impairment or with end-stage renal disease. Patients with end stage renal disease on dialysis may have lower exposure than expected. Exercise extreme caution in patients especially with severe renal impairment or ESRD, since fatal renal failure has been reported with sunitinib. Subsequent dosing should be based on tolerability.

## Dosage in the Elderly

Dose modification not required.

## Children:

Safety and effectiveness in children have not been established. Reversible, dose-related physeal dysplasia has been reported in animal models.

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## F - Adverse Effects

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

| **Very common (≥ 50%)** | **Common (25-49%)** | **Less common (10-24%)** | **Uncommon (< 10%),<br><br>but may be severe or life-threatening** |
|---|---|---|---|
| • Increased LFTs (may be severe)<br>• Increased creatinine (may be severe)<br>• Diarrhea<br>• Fatigue<br>• Increased amylase (may be severe)<br>• Nausea, vomiting | • Increased CPK (may be severe)<br>• Dysgeusia<br>• Abnormal electrolytes<br>• Dyspepsia<br>• Mucositis<br>• Anorexia, weight loss<br>• Skin discolouration<br>• Rash (may be severe)<br>• Abdominal pain<br>• Hand-foot syndrome<br>• Hypertension (may be severe)<br>• Hair depigmentation<br>• Hemorrhage<br>• Left-ventricular dysfunction (may be severe) | • Respiratory disorders<br>• Myelosuppression +/- infection (may be severe, including viral/fungal)<br>• Hyper or hypoglycemia<br>• Constipation<br>• Headache<br>• Dizziness<br>• Hypothyroidism<br>• Musculoskeletal pain<br>• Insomnia<br>• Psychiatric disorders<br>• Eye disorders | • Arterial thromboembolism<br>• Venous thromboembolism<br>• Arrhythmia, prolonged QT<br>• Artery aneurysm / dissection<br>• GI fistula or perforation<br>• Disseminated intravascular coagulation<br>• Hemolysis<br>• Idiopathic thrombocytopenic purpura<br>• Hypersensitivity<br>• Radiation dermatitis<br>• Wound dehiscence<br>• Cholecystitis<br>• Necrotizing fasciitis<br>• Adrenal insufficiency<br>• Hyperthyroidism<br>• Tumour lysis syndrome<br>• Osteonecrosis of the jaw<br>• Rhabdomyolysis<br>• PRES, seizure<br>• Nephrotic syndrome<br>• Pleural effusion |

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## G - Interactions

Refer to SUNItinib drug monograph(s) for additional details

- Consider sunitinib dosage adjustment with strong inhibitors and inducers of CYP3A4; avoid if possible
- Avoid concomitant use with drugs that prolong the QT interval
- Avoid combining with bevacizumab given increased risk of toxicity
- Use with caution with drugs that cause hypoglycemia; may need dosage adjustment of hypoglycemic drug

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## H - Drug Administration and Special Precautions

Refer to SUNItinib drug monograph(s) for additional details

### Administration

- Prescribed dose should be administered orally, once daily with or without food.
- Avoid any grapefruit, starfruit, Seville oranges or their juices/products while on this treatment. (See interactions)
- Store at room temperature (15-30°C).

### Contraindications

- patients who have a hypersensitivity to this drug or any of its components
- patients with uncontrolled hypertension, abnormal ↑QT or AV block

### Other Warnings/Precautions

- Extreme caution should be exercised in patients at increased risk of torsade de pointes, with bradycardia, QTc prolongation, cardiac or thromboembolic risk factors, electrolyte disturbances, and in patients taking medications which prolong QTc or the PR interval.
- Patients who had, within 12 months, cardiovascular events such as MI (including severe/unstable angina), coronary/peripheral artery bypass graft, symptomatic CHF, CVA, TIA or pulmonary embolism were excluded from clinical trials. The risk versus benefit of sunitinib

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use should be carefully considered in these patients
- Concomitant use of warfarin or antiplatelet agents should be avoided.
- Hypoglycemia has been reported in both diabetic and non-diabetic patients while on sunitinib and may be severe.
- Patients with intra-abdominal malignancies are at an increased risk of perforation.
- Subclinical adrenal insufficiency may occur and stressed patients (surgery, trauma, etc.) should be monitored carefully.
- Hold treatment in patients undergoing major surgical procedures. The timing of restarting sunitinib should be based on clinical judgment of recovery.

**Pregnancy and lactation:**

- Sunitinib is contraindicated in pregnancy. Females of childbearing potential and male patients should use effective contraception during treatment and for at least 6 months after treatment cessation (general recommendation).
- Breastfeeding is not recommended.

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## I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

Recommended Clinical Monitoring

- Blood glucose; baseline and periodic; closer monitoring in diabetic patients may be needed
- CBC; baseline and before each cycle
- Dental evaluation; before starting treatment with preventative dentistry as needed
- ECG; baseline and periodic during therapy
- Liver function tests, with lipase and amylase; baseline and at each cycle
- LVEF in patients with cardiac risk factors; baseline and regular
- Renal function tests and electrolytes (including Mg, Ca, PO4); baseline and at each cycle
- Thyroid function tests; baseline then q3 months, and as clinically indicated
- Urinalysis; baseline and periodic
- Blood pressure and assessment for signs and symptoms of pancreatitis, hypo-/hyperthyroidism, hypertension, myopathy, delayed wound healing, TLS, thromboembolism, bleeding, cardiovascular, neurologic, GI or respiratory effects, adrenal insufficiency (especially with stress); regular

- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

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Suggested Clinical Monitoring

- Adrenal function tests in patients who experience stress (surgery, trauma, severe infection)

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## J - Administrative Information

Outpatient prescription for home administration

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## K - References

Cella D, Michaelson MD, Bushmakin AG, et al. Health-related quality of life in patients with metastatic renal cell carcinoma treated with sunitinib vs interferon-alpha in a phase III trial: final results and geographical analysis. Br J Cancer 2010 ; 102(4) : 658-64.

Lee JL, Kim MK, Park I, et al. RandomizEd phase II trial of Sunitinib four weeks on and two weeks off versus Two weeks on and One week off in metastatic clear-cell type REnal cell carcinoma: RESTORE trial. Ann Oncol. 2015 Nov;26(11):2300-5.

Motzer RJ, Hutson TE, Tomczak P, et al. Overall Survival and Updated Results for Sunitinib Compared With Interferon Alfa in Patients With Metastatic Renal Cell Carcinoma. J Clin Oncol 2009; 27: 3584-90.

Motzer RJ, Hutson TE, Tomczak P, et al. Sunitinib versus Interferon Alfa in Metastatic Renal-Cell Carcinoma. N Engl J Med 2007; 356: 115-24.

Sunitinib drug monograph, Cancer Care Ontario.

**PEBC Advice Documents or Guidelines**

- The Use of Targeted Therapies in Patients with Inoperable Locally Advanced or Metastatic Renal Cell Cancer

**October 2020** Modified Uncommon Adverse Effects and Monitoring sections

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## M - Disclaimer

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***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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