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	Gastrointestinal - Neuroendocrine (GI)
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	The treatment of patients with unresectable locally advanced or metastatic, well differentiated pancreatic neuroendocrine tumours (pancreatic NET), whose disease is progressive. Additional criteria for funding: Well- or moderately-differentiated, good performance status (ECOG 0 to 2), no prior everolimus.
Supplementary Public Funding	**SUNItinib** Exceptional Access Program (SUNItinib - For patients who have progressive, unresectable, well or moderately differentiated, locally advanced or metastatic pancreatic neuroendocrine tumours (pNET), according to specific criteria) (EAP Website)

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B - Drug Regimen

SUNItinib	37.5 to 50 mg	PO	Days 1 to 28

(Outpatient prescription in multiples of 12.5mg, 25mg, 37.5mg and 50mg capsules)

Alternative Schedule:

SUNItinib	37.5 mg	PO	Daily

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C - Cycle Frequency

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

Alternative schedule: CONTINUOUS

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 37.5 mg nor be decreased below 25mg. Doses should be held prior to surgery

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

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Dosage with toxicity

Toxicity	Action	Dose
Severe hypertension	Hold and treat appropriately.	May resume only if hypertension is controlled. (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.

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).

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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.

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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%), but may be severe or life-threatening
• Increased LFTs (may be severe) • Increased creatinine (may be severe) • Diarrhea • Fatigue • Increased amylase (may be severe) • Nausea, vomiting	• Increased CPK (may be severe) • Dysgeusia • Abnormal electrolytes • Dyspepsia • Mucositis • Anorexia, weight loss • Skin discolouration • Rash (may be severe) • Abdominal pain • Hand-foot syndrome • Hypertension (may be severe) • Hair depigmentation • Hemorrhage • Left-ventricular dysfunction	• Respiratory disorders • Myelosuppression +/- infection (may be severe, including viral/fungal) • Hyper or hypoglycemia • Constipation • Headache • Dizziness • Hypothyroidism • Musculoskeletal pain • Insomnia • Psychiatric disorders • Eye disorders	• Arterial thromboembolism • Venous thromboembolism • Arrhythmia, prolonged QT • Artery aneurysm / dissection • GI fistula or perforation • Disseminated intravascular coagulation • Hemolysis • Idiopathic thrombocytopenic purpura • Hypersensitivity • Radiation dermatitis • Wound dehiscence • Cholecystitis • Necrotizing fasciitis

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	(may be severe)		• Adrenal insufficiency • Hyperthyroidism • Tumour lysis syndrome • Osteonecrosis of the jaw • Rhabdomyolysis • PRES, seizure • Nephrotic syndrome • Pleural effusion

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G - Interactions

Refer to SUNItinib drug monograph(s) for additional details

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H - Drug Administration and Special Precautions

Refer to SUNItinib drug monograph(s) for additional details

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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 at 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

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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); at each visit

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

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

Kulke MH, Lenz H-F, Meropol NJ, Posey J, Ryan DP, et al. Activity of Sunitinib in Patients With Advanced Neuroendocrine Tumors. J Clin Oncol 2008; 26:3403-3410.

Raymond E, Dahan L, Raoul J-L, et al. Sunitinib Malate for the Treatment of Pancreatic Neuroendocrine Tumors. New Eng J Med. 2011; 364(6):501-513.

Strosberg JR, Weber JM, Choi J, et al. A phase II clinical trial of sunitinib following hepatic transarterial embolization for metastatic neuroendocrine tumors. Ann Oncol 2012;;23(9):2335-41.

Sunitinib drug monograph, Cancer Care Ontario.

PEBC Advice Documents or Guidelines

- Systemic Therapy of Incurable Gastroenteropancreatic Neuroendocrine Tumours

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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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