

## Regimen Monograph

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### A - Regimen Name

# SELP Regimen

selpercatinib

**Disease Site** Endocrine  
Thyroid

**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**

- Third or subsequent line treatment in advanced or metastatic RET fusion-positive differentiated thyroid carcinoma (DTC)
- Second line treatment in unresectable advanced or metastatic RET-mutant medullary thyroid cancer (MTC)

(Refer to EAP for detailed funding criteria)

**Supplementary  
Public Funding**

**[selpercatinib](#)**

Exceptional Access Program (selpercatinib - For the treatments of advanced or metastatic RET fusion-positive differentiated thyroid carcinoma (DTC); and unresectable advanced or metastatic RET-mutant medullary thyroid cancer (MTC)) ([EAP Website](#))

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**B - Drug Regimen**

**Patients with Body Weight (BW) < 50 kg:**

<a href="#">selpercatinib</a>	120 mg	PO	BID (every 12 hours)
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**Patients with Body Weight (BW) ≥ 50 kg:**

<a href="#">selpercatinib</a>	160 mg	PO	BID (every 12 hours)
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**C - Cycle Frequency**

**CONTINUOUS TREATMENT**

Until clinically meaningful disease progression\* or unacceptable toxicity

(\*Refer to CADTH recommendations and Wirth et al)

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## D - Premedication and Supportive Measures

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

- Also refer to [CCO Antiemetic Recommendations](#).

**Screen for hepatitis B virus in all cancer patients starting systemic treatment.** Refer to the [hepatitis B virus screening and management](#) guideline.

**Other Supportive Care:**

- Consider appropriate prophylaxis including hydration for patients at risk of tumour lysis syndrome (e.g. rapidly growing tumors, high tumor burden, renal dysfunction, or dehydration).

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## E - Dose Modifications

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

Confirm RET gene fusion or mutation using a validated test before initiation.

Hypertension should be well-controlled prior to initiation of treatment.

Patients must have a QTcF interval of  $\leq 470$  ms and serum electrolytes within normal range before starting treatment.

Hold selpercatinib for  $\geq 7$  days prior to elective surgery. Do not administer for  $\geq 2$  weeks following major surgery and until adequate wound healing.

Refer to Interactions section for dosing recommendations when co-administered with **CYP3A4 inhibitors**.

### Dosage with toxicity

Dose Levels	Selpercatinib Dose < 50 kg BW	Selpercatinib Dose $\geq 50$ kg BW
0	120 mg twice daily	160 mg twice daily
-1	80 mg twice daily	120 mg twice daily
-2	40 mg twice daily	80 mg twice daily
-3	40 mg <b>once</b> daily	40 mg twice daily
-4	Discontinue	Discontinue

Toxicity	Severity	Action
QT Prolongation	Grade 3	<p>Hold until resolved to Grade 1 or baseline.</p> <p>Resume at 1 dose level ↓.</p> <p>If recurs despite <b>2</b> dose reductions, discontinue.</p>
	Grade 4 or signs and symptoms of serious arrhythmia	Discontinue.
↑ AST or ALT	Grade 3 or 4	<p>Hold until resolved to Grade 1 or baseline; monitor AST or ALT weekly.</p> <p>Resume at <b>2</b> dose levels ↓; continue AST or ALT weekly monitoring.</p> <p>Increase by 1 dose level after ≥ 2 weeks without recurrence, and then increase to dose taken prior to the onset of toxicity after ≥ 4 weeks without recurrence. Continue AST or ALT weekly monitoring for 4 weeks thereafter.</p> <p>If recurs despite dose reductions, discontinue.</p>
Hypersensitivity	Any	<p>Hold until resolved; begin steroid treatment.</p> <p>Resume at <b>3</b> dose levels ↓ while continuing steroid treatment.</p> <p>Increase selpercatinib by 1 dose level weekly if no recurrence.</p> <p>Taper steroid dose after selpercatinib has been tolerated for ≥ 7 days at the dose taken prior to the onset of toxicity.</p> <p>If recurs despite dose reductions, discontinue.</p>
Hypertension	Grade 3	<p>Hold until controlled with medical management.</p> <p>Resume at 1 dose level ↓.</p>
	Grade 4 or significant hypertension that cannot be controlled with antihypertensive therapy	Discontinue.

Hemorrhagic Events	Grade 3 or 4	Hold until resolved to $\leq$ Grade 1 or baseline. Discontinue for severe or life-threatening events.
Interstitial Lung Disease / Pneumonitis	Grade 2 that does not resolve to baseline or grade 1 within 7 days (despite maximal supportive measures)	Hold until resolved to Grade 1 or baseline. Resume at 1 dose level ↓.
	Grade 3 or 4	Discontinue.
Other Adverse Reactions	Grade 3 or 4	Hold until resolved to $\leq$ Grade 1 or baseline. Resume at a reduced dose.

### **Hepatic Impairment**

Limited safety data are available in patients with severe hepatic impairment; monitor ALT and AST more frequently as clinically indicated.

<b>Hepatic Impairment</b>	<b>Selpercatinib Dose (regardless of BW)</b>
Child-Pugh class A or B	No dose adjustment
Child-Pugh class C	80 mg twice daily

### **Renal Impairment**

No dosage adjustment is necessary in patients with mild, moderate or severe renal impairment. Selpercatinib is not recommended in patients with end-stage renal disease.

### **Dosage in the Elderly**

No overall differences in safety or efficacy observed between patients  $\geq$  65 years of age and younger patients.

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## F - Adverse Effects

Refer to [selpercatinib](#) 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
<ul style="list-style-type: none"> <li>• Edema</li> <li>• Diarrhea</li> </ul>	<ul style="list-style-type: none"> <li>• Fatigue</li> <li>• Dry mouth</li> <li>• Hypertension (may be severe)</li> <li>• ↑ LFTs (may be severe)</li> <li>• Rash</li> <li>• Abdominal pain</li> <li>• Constipation</li> <li>• Nausea, vomiting</li> <li>• Headache</li> <li>• Cough, dyspnea</li> </ul>	<ul style="list-style-type: none"> <li>• Hemorrhage (may be severe)</li> <li>• Musculoskeletal pain</li> <li>• Anorexia, weight loss</li> <li>• Dizziness</li> <li>• QT interval prolonged (may be severe)</li> <li>• Abnormal electrolyte(s)</li> <li>• Mucositis</li> <li>• Myelosuppression ± infection</li> <li>• Erectile dysfunction</li> <li>• Hypothyroidism</li> <li>• Insomnia</li> <li>• ↓ albumin</li> <li>• Ascites</li> <li>• Pleural effusion</li> <li>• ↑ Bilirubin</li> <li>• Weight gain</li> <li>• Alopecia</li> </ul>	<ul style="list-style-type: none"> <li>• Atrial fibrillation</li> <li>• Venous thromboembolism</li> <li>• Pericardial effusion</li> <li>• Pleural effusion</li> <li>• Pneumonitis</li> <li>• Hypersensitivity</li> <li>• Creatinine increased</li> <li>• Chylothorax</li> <li>• Tumour lysis syndrome</li> </ul>

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## G - Interactions

Refer to [selpercatinib](#) drug monograph(s) for additional details.

- Avoid concomitant use with strong or moderate CYP3A4 inhibitors. If unavoidable, ↓ selpercatinib dose and perform ECG more frequently. Refer to table below.
- Avoid concomitant use with strong or moderate CYP3A4 inducers.
- Avoid concomitant use with sensitive CYP3A4 or CYP2C8 substrates. If unavoidable, ↓ substrate dose as per product monograph.
- Avoid coadministration with PPIs. If unavoidable, administer selpercatinib with food.
- Avoid coadministration with H2 receptor antagonists. If unavoidable, administer selpercatinib 2 hours before or 10 hours after H2 receptor antagonist.
- Avoid coadministration with antacids. If unavoidable, administer selpercatinib 2 hours before or 2 hours after antacids.
- Avoid concomitant use with BCRP or P-gp substrates with a narrow therapeutic range. If unavoidable, follow recommendations for BCRP or P-gp substrates as per product monograph.
- Avoid concomitant use with drugs that may prolong QT. If unavoidable, monitor ECG and electrolytes.
- Avoid concomitant use with drugs that disrupt electrolyte levels, if possible.
- Avoid concomitant use with drugs that reduce heart rate.

### Dose Modification when Co-administered with CYP3A4 Inhibitors

Planned Selpercatinib Dose (mg twice daily)	Selpercatinib Dose (mg twice daily)	
	with Moderate CYP3A4 inhibitor*	with Strong CYP3A4 inhibitor*
120	80	40
160	120	80

\*After the inhibitor has been discontinued for 3 to 5 elimination half-lives of the inhibitor, resume selpercatinib at the dose taken before starting the CYP3A4 inhibitor.

There is no data on the safety of concomitant use of CYP3A inhibitors in patients whose dose was previously reduced due to adverse effects.

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## H - Drug Administration and Special Precautions

Refer to [selpercatinib](#) drug monograph(s) for additional details.

### Administration

- Administer selpercatinib with or without food. Refer to Interaction section when given concomitantly with PPIs, H2 receptor antagonists, or antacids.
- Capsules should be swallowed whole with a glass of water and not opened, crushed, or chewed.
- Grapefruit, starfruit, Seville oranges, their juices or products should be avoided during selpercatinib treatment.
- If a dose is missed, the dose may be taken if there are  $\geq 6$  hours until the next dose. If there are  $< 6$  hours until the next dose, the dose should be skipped and the next dose should be taken at the scheduled time. Patients should not take 2 doses at the same time to make up for a missed dose.
- If the patient vomits after taking a dose, an additional dose should not be taken. The next dose should be continued as scheduled.
- Store at room temperature (15° to 30°C).

### Contraindications

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

### Other Warnings/Precautions

- Avoid use of selpercatinib in patients with conditions that may increase the risk of experiencing torsade de pointes.
- Patients should exercise caution when driving or operating a vehicle or potentially dangerous machinery as dizziness has been reported.

### Pregnancy/Lactation

- This regimen is not recommended for use in pregnancy. Adequate contraception should be used by patients and their partners while on treatment and after the last treatment dose. Recommended methods and duration of contraception may differ depending on the treatment. Refer to the drug monograph(s) for more information.
- Breastfeeding is not recommended during this treatment and after the last treatment dose. Refer to the drug monograph(s) for recommendations after the last treatment dose (if available).
- Fertility effects: Probable

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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.

Refer to the [hepatitis B virus screening and management](#) guideline for monitoring during and after treatment.

### Recommended Clinical Monitoring

- Liver function tests; Baseline, every 2 weeks for 3 months after initiation, then monthly, and as clinically indicated.
- ECG; Baseline, 1 week after initiation, then monthly for 6 months, and as clinically indicated
- Electrolytes, including K, Mg, Ca; Baseline, 1 week after initiation, then monthly for 6 months, and as clinically indicated
- Blood pressure; Baseline, 1 week after initiation, then monthly for 6 months, and as clinically indicated
- CBC; Baseline, monthly and as clinically indicated
- Thyroid function tests; Baseline and as clinically indicated
- Renal function tests\*; Baseline and as clinically indicated
- Clinical toxicity assessment for hypersensitivity, pneumonitis, TLS, infection, bleeding, delayed wound healing (if applicable), GI, and cardiovascular effects; At each visit
- Grade toxicity using the current [NCI-CTCAE \(Common Terminology Criteria for Adverse Events\) version](#)

\*Selpercatinib may increase serum creatinine, without affecting glomerular function, by inhibiting renal tubular secretion transporters. Consider alternative markers that are not based on creatinine (e.g. BUN) for determining renal function

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## J - Administrative Information

Outpatient prescription for home administration

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## K - References

CADTH reimbursement recommendation: selpercatinib (RET-fusion positive differentiated thyroid carcinoma with advanced or metastatic disease). July 2022.

CADTH reimbursement recommendation: selpercatinib (unresectable advanced or metastatic RET-mutant medullary thyroid cancer). October 2022.

Selpercatinib drug monograph. Ontario Health (Cancer Care Ontario).

Wirth LJ, Sherman E, Robinson B, . Efficacy of selpercatinib in *RET*-altered thyroid cancers. N Engl J Med. 2020 Aug 27;383(9):825-35.

### **PEBC Advice Documents or Guidelines**

- [CCO Thyroid Cancer Guideline: An Endorsement of the 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer](#)

**April 2025** Expanded into full regimen monograph

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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.*

*The information set out in the drug monographs, regimen monographs, appendices and symptom management information (for health professionals) contained in the Drug Formulary (the “Formulary”) is intended for healthcare providers and is to be used for informational purposes only. The information is not intended to cover all possible uses, directions, precautions, drug interactions or adverse effects of a particular drug, nor should it be construed to indicate that use of a particular drug is safe, appropriate or effective for a given condition. The information in the Formulary is not intended to constitute or be a substitute for medical advice and should not be relied upon in any such regard. All uses of the Formulary are subject to clinical judgment and actual prescribing patterns may not follow the information provided in the Formulary.*

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*Some Formulary documents, such as the medication information sheets, regimen information sheets and symptom management information (for patients), are intended for patients. Patients should always consult with their healthcare provider if they have questions regarding any information set out in the Formulary documents.*

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