

Regimen Monograph

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A - Regimen Name

EVER Regimen

Everolimus

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

- For the treatment of patients who have progressive, unresectable, well or moderately differentiated, locally advanced or metastatic pancreatic neuroendocrine tumors (pNET). Funded for patients with ECOG 0-2 who have not had disease progression while taking sunitinib.
- For the treatment of unresectable, locally advanced or metastatic, well-differentiated non-functional neuroendocrine tumours (NETs) of gastrointestinal origin in patients with ECOG 0-2 and progressive disease.

**Supplementary
Public Funding****[everolimus](#)**

Exceptional Access Program (everolimus - For patients who have progressive, unresectable, well or moderately differentiated, locally advanced or metastatic pancreatic neuroendocrine tumors (PNET), with specific criteria) ([EAP Website](#))

[everolimus](#)

Exceptional Access Program (everolimus - Treatment of unresectable, locally advanced or metastatic, well-differentiated non-functional neuroendocrine tumours (NETs) of GI or lung origin, according to clinical criteria) ([EAP Website](#))

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B - Drug Regimen**[everolimus](#)**

10 mg

PO

Daily

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C - Cycle Frequency**CONTINUOUS TREATMENT**

Until disease progression, no evidence of further response, or unacceptable toxicity.

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D - Premedication and Supportive Measures

Antiemetic Regimen: Minimal – 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:

- Manage stomatitis with non-irritant oral rinses. Antifungal agents should not be used unless an oral fungal infection has been diagnosed.
- Consider the use of PJP prophylaxis when concomitant use of corticosteroids or other immunosuppressants are required.

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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.

Do not use for the treatment of carcinoid tumours. Patients in whom drug-drug interactions are likely (and who cannot discontinue the concomitant medication) may require dose modification (refer to Interactions section for details). Optimal glycemic/lipidemic control must be obtained prior to starting therapy.

Prophylaxis for PJP should be considered when concurrent use of corticosteroids or other immunosuppressive agents are required.

Dose levels: 10mg daily, 5mg daily, 5mg q2d

Dosage with toxicity

<u>Toxicity</u>	<u>Grade 1</u>	<u>Grade 2</u>	<u>Grade 3</u>	<u>Grade 4</u>
Non-infectious pneumonitis	If tolerable, maintain same dose. Monitor and treat patient appropriately.	Consider hold until ≤ grade 1. Rule out infection and then consider corticosteroids. Restart with 1 dose level ↓. Discontinue if no recovery within 4 weeks.	Hold until ≤ grade 1. Rule out infection and then consider corticosteroids. Restart with 1 dose level ↓. Discontinue if grade 3 recurs.	Discontinue, investigate and treat patient appropriately.
Stomatitis		Hold until ≤ grade 1 and restart at same dose. If recurs, hold until ≤ grade 1 and restart with 1 dose level ↓.	Hold until ≤ grade 1 and restart with 1 dose level ↓.	
Metabolic events (e.g. hyperglycemia, hyperlipidemia)*		Maintain same dose. Monitor and start appropriate therapy.	Hold until ≤ grade 1 and restart with 1 dose level ↓. Monitor and start appropriate therapy.	
Other related non-hematologic toxicities		Maintain same dose if tolerable. If intolerable, hold until ≤ grade 1 and restart at same dose. If recurs, hold until ≤ grade 1 and restart with 1 dose level ↓.	Hold until ≤ grade 1 and restart with 1 dose level ↓. Consider discontinuing if recurs.	

* consider urgent therapy if hypertriglyceridemia due to risk of pancreatitis

Hepatic Impairment

Hepatic impairment (baseline and during treatment)	Everolimus dose (adults)
Mild (Child-Pugh class A)	7.5mg once daily. ↓ to 5mg daily if not well tolerated
Moderate (Child-Pugh class B)	5mg daily. ↓ to 2.5 mg daily if not well tolerated
Severe (Child-Pugh class C)	Use only when benefits outweigh risks, at 2.5 mg daily

Renal Impairment

No dose adjustment required.

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F - Adverse Effects

Refer to [everolimus](#) drug monograph(s) for additional details of adverse effects

Most Common Side Effects	Less Common Side Effects, but may be Severe or Life-Threatening
<ul style="list-style-type: none"> • Mucositis • Fatigue • Diarrhea • Rash • Nausea, vomiting • Anorexia • Fluid retention (may be severe) • ↑ LFTs • Pneumonitis (may be severe) • Myelosuppression ± bleeding, infection (may be severe, includes opportunistic infections) • Hyperglycemia • Hyperlipidemia 	<ul style="list-style-type: none"> • Nephrotoxicity • Cardiotoxicity • Hypersensitivity, including angioedema • Venous thromboembolism • Delayed wound healing • Hypertension • Rhabdomyolysis • GI obstruction • Pure red cell aplasia

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G - Interactions

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

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H - Drug Administration and Special Precautions

Refer to [everolimus](#) 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.

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

Recommended Clinical Monitoring

- CBC; baseline and periodic
- Fasting blood glucose and lipids; baseline and periodic (more frequent with concomitant use of drugs that can cause hyperglycemia)
- Liver function tests; baseline and periodic
- Renal function tests, electrolytes (including Ca, Mg and PO₄), urinalysis; baseline and periodic
- Clinical assessment of mucositis, fatigue, fluid retention, pulmonary toxicity, infection, rash, diarrhea, bleeding, thromboembolism, rhabdomyolysis; regular
- Grade toxicity using the current [NCI-CTCAE \(Common Terminology Criteria for Adverse Events\) version](#)

Suggested Clinical Monitoring

- Pulmonary function tests in patients with significant lung disease; baseline

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J - Administrative Information

Outpatient prescription for home administration

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K - References

Everolimus drug monograph, Cancer Care Ontario.

Yao JC, Fazio N, Singh S, et al. RAD001 in Advanced neuroendocrine tumours, fourth trial (RADIANT-4) study group. Everolimus for the treatment of advanced, non-functional neuroendocrine tumours of the lung or gastrointestinal tract (RADIANT-4): a randomised, placebo-controlled, phase 3 study. Lancet 2016 Mar 5;387(10022):968-77.

Yao J, Shah, M, Tetsuhide I, et al. Everolimus for advanced pancreatic neuroendocrine tumours. N Engl J Med 2011; 364: 514-23.

PEBC Advice Documents or Guidelines

- [Systemic Therapy for Unresectable Advanced or Metastatic Pancreatic and Midgut Neuroendocrine Tumours](#)

June 2024 Updated PEBC guideline link

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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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