Regimen Monograph

A - Regimen Name

EVER Regimen

Everolimus

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 metastatic renal cell carcinoma, as second- or third-line therapy in patients previously treated with a funded tyrosine kinase inhibitor

Supplementary Public Funding
everolimus
Exceptional Access Program (everolimus - Treatment of metastatic renal cell carcinoma (mRCC) as second or third line therapy in patients previously treated for mRCC with a funded tyrosine kinase inhibitor (TKI), with specific 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.

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.

Consider the use of PJP prophylaxis when concomitant use of corticosteroids or other immunosuppressants are required.

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

Dosage with toxicity

Toxicity	Grade 1	Grade 2	Grade 3	Grade 4
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 for 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
• 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	• 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 PO_4), 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

Motzer RJ, Escudier B, Oudard S, et al. Phase 3 trial of everolimus for metastatic renal cell carcinoma: final results and analysis of prognostic factors. Cancer 2010;116(18):4256-65.

Motzer RJ, Escudier B, Oudard S, et al. Efficacy of everolimus in advanced renal cell carcinoma: a double-blind, randomised, placebo-controlled phase III trial. Lancet 2008; 372: 449-56.

PEBC Advice Documents or Guidelines

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

March 2023 Updated Rationale/uses section

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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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