Regimen Monograph

A - Regimen Name

TEMS Regimen

Temsirolimus

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. It is recommended and funded for first-line, poor-risk (defined by Mekhail criteria) metastatic renal cell cancer.

Supplementary Public Funding
temsirolimus
New Drug Funding Program (Temsirolimus - Metastatic Renal Cell Carcinoma)

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B - Drug Regimen

temsirolimus	25 mg	IV	Weekly

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C - Cycle Frequency

REPEAT WEEKLY

Until disease progression or unacceptable toxicity

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D - Premedication and Supportive Measures

Antiemetic Regimen: Minimal

Other Supportive Care:

- 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.

Pre-medications (prophylaxis for infusion reaction):

- Diphenhydramine 25 to 50mg IV (or equivalent) should be given 30 minutes before the start of the infusion.

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E - Dose Modifications

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

Do not administer if bilirubin > 1.5 x ULN.

Dosage with toxicity

Toxicity and Grade	Action	Dose
Pneumonitis (grade 1 or 2)	Hold until ≤ grade 1; may continue if asymptomatic. Consider steroids.	Consider dose reduction (by 5mg/week)*
Pneumonitis (grade 3 or 4)	Discontinue, consider steroids	Discontinue permanently
Intolerable grade 2 non-hematological	May continue AND	Reduce by 5mg/week*
Grade 3 or 4 non-hematological	Hold until recovered to ≤ grade 2 AND	Reduce by 5mg/week*
Platelet < 75 x 10^9/L and/or ANC < 1 x 10^9/L	Hold until recovery to ≥ 75 x 10^9/L and ≥1 x 10^9/L AND	Reduce by 5mg/week*

*Minimum dose is 15mg/week

Management of Infusion-related reactions:

Also refer to the CCO guideline for detailed description of Management of Cancer Medication-Related Infusion Reactions.

Grade	Action
1 or 2	• Stop the infusion and observe the patient for at least 30-60 minutes. • If deemed appropriate by the physician, temsirolimus may be resumed. • Administer a H_1-receptor antagonist if one was not previously administered and/or a H_2-receptor antagonist, such as famotidine 20mg IV or ranitidine 50mg IV, approximately 30 minutes before restarting the infusion. • Restart at a slower rate of up to 60 minutes.
3 or 4	• Stop the infusion. Treat symptoms with antihistamines, antipyretics, beta-agonists and/or corticosteroids as appropriate. Consider discontinuing temsirolimus treatment.

Hepatic Impairment

Hepatic metabolism is significant.

	AST	Bilirubin	Action
Mild	> ULN	≤ ULN	Caution. Dose at 15mg
		>1 - 1.5 x ULN	Caution. Dose at 15mg
Moderate to severe		>1.5 x ULN	Do not treat.

Renal Impairment

Use with caution. No formal studies have been performed in renally impaired patients. Dose adjustment may not be required since <5% of the dose is excreted in the urine. Temsirolimus use in hemodialysis was described in a case series.

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F - Adverse Effects

Refer to temsirolimus 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
• Hyperglycemia • Hyperlipidemia • ↑ LFTs (may be severe) • Creatinine increased (may be severe) • Fatigue	• Rash (may be severe) • Edema (may be severe) • Mucositis • Nausea and vomiting • Anorexia • Infection (including opportunistic) • Cough, dyspnea • Diarrhea • Hemorrhage (may be severe) • Abnormal electrolytes	• Abdominal pain • Constipation • Musculoskeletal pain • Myelosuppression • Nail changes • Dysguesia • Insomnia	• Hypersensitivity • Venous thromboembolism • GI perforation • Delayed wound healing • QT interval prolonged • Rhabdomyolysis and ↑ CPK • Seizure • Interstitial lung disease • Secondary malignancy

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G - Interactions

Refer to temsirolimus drug monograph(s) for additional details.

- Avoid concomitant usage with CYP3A4/5 inducers or strong CYP3A4 inhibitors.
- Caution and monitor for toxicity with CYP3A4/5, CYP2D6 and Pgp substrates.
- Extreme caution with anticoagulants due to increased risk of CNS bleeding in patients with CNS tumours.
- Caution with ACE inhibitors or calcium channel blockers due to increased risk of angioneurotic edema.
- Avoid QT prolonging drugs if possible.

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H - Drug Administration and Special Precautions

Refer to temsirolimus drug monograph(s) for additional details.

Administration:

- Inject supplied diluent (contains polysorbate 80 and PEG 400) into the drug vial and then dilute further in 250mL Normal Saline, infuse over 30 -60 minutes. Avoid excessive shaking as this may cause foaming.
- To decrease di-(2-ethylhexyl) phthalate (DEHP) leaching or avoid excessive drug loss, materials used in administration must be composed of glass, polyolefin or polyethylene. Use a non-PVC non-DEHP tubing, including an in-line polyethersulfone filter ≤ 5 microns. A polyethersulfone end-filter (0.2 to 5 microns) may be added if the administration set does not have an in-line filter component. The use of both an in-line and end-filter is not recommended.
- The drug concentrate-diluent mixture is stable for up to 24 hours at room temperature and protected from light. The final diluted drug solution should be completely administered within 6 hours from the time that the concentrate-diluent mixture is added to the Normal Saline bag.
- Keep unopened drug and diluent vials refrigerated (2-8°C); do not freeze.
- Protect the drug and diluted solutions from light. Do not use if drug is discoloured or if particulates are present.

Contraindications:

- patients with known hypersensitivity to this sirolimus, temsirolimus, or any ingredients in the formulation
- patients with elevated bilirubin (> 1.5 x ULN)

Other Warnings/Precautions:

- patients with pre-existing or at risk of prolonged QTc
- patients with brain metastases (increased risk of bleeding)
- patients who have known hypersensitivity to an antihistamine or cannot receive an antihistamine for other medical reasons
- patients on anticoagulants or who have had recent surgery
- avoid use of live vaccines

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

- CBC; Baseline and weekly
- Fasting glucose; Baseline and weekly
- Liver function tests; Baseline and every 2 weeks
- Renal function tests & electrolytes; Baseline and every 2 weeks
- Lipids; Baseline and monthly
- Routine assessment for signs and symptoms of fatigue, hyperglycemia, bleeding, pneumonitis, fluid retention, skin toxicity, infections, mucositis, delayed wound healing, infusion reactions, rhabdomyolysis (especially with statins).; At each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

Suggested Clinical Monitoring

- Radiologic screening for ILD; baseline and periodic

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J - Administrative Information

Approximate Patient Visit	1 to 1.5 hours
Pharmacy Workload (average time per visit)	17.283 minutes
Nursing Workload (average time per visit)	39.167 minutes

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K - References

Hudes G, Carducci M, Tomczak P, et al. Temsirolimus, Interferon Alfa, or Both for Advanced Renal-Cell Carcinoma. N Engl J Med 2007;356:2271-81.

Mekhail TM, Abou-Jawde RM, BouMerhi G, et al. Validation and extension of the Memorial Sloan-Kettering prognostic factors model for survival in patients with previously untreated metastatic renal cell carcinoma. J Clin Oncol. 2005;23:832-41.

Temsirolimus drug monograph, Ontairo Health (Cancer Care Ontario).

PEBC Advice Documents or Guidelines

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

June 2024 Modified Interactions, Pregnancy/Lactation, and Monitoring sections

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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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