Regimen Monograph

A - Regimen Name

AXIT Regimen

Axitinib

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 advanced metastatic renal cell carcinoma:

- As second line therapy in patients with disease in any risk category after failure to sunitinib or pazopanib
- As third line therapy in patients in the intermediate or poor risk disease category, who have progressed on combination therapy with ipilimumab and nivolumab as first line and sunitinib or pazopanib as second line

(Refer to EAP for details on funding criteria)

Supplementary Public Funding

aXitinib
Exceptional Access Program (aXitinib - For second or third line treatment of advanced renal cell carcinoma, according to clinical criteria)

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B - Drug Regimen

aXitinib*	5 mg	PO	BID

* may be titrated up to a maximum of 10 mg twice daily according to tolerance. Refer to section E - Dose Modifications for dose levels.

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C - Cycle Frequency

CONTINUOUS TREATMENT

Until disease progression, in the absence of 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.

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E - Dose Modifications

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

Do not start treatment until any hypertension is controlled and platelets are ≥ 100 x 10^9/L and ANC ≥ 1.5 x 10^9/L.

Correct electrolyte abnormalities prior to treatment, especially potassium, calcium and magnesium.

Hold axitinib for at least 24 hours prior to planned surgery. Re-start post-surgery based on clinical assessment of wound healing.

Dosage with toxicity

Dose Level	Dose
+2	10 mg BID
+1	7 mg BID*
0 (starting dose)	**5 mg BID***
-1	3 mg BID
-2	2 mg BID

*May ↑ 1 dose level in patients who tolerate (≤ grade 2 toxicity) the current dose for 2 consecutive weeks, with no prior dose modification, normotensive and do not require antihypertensive medications

Do not re-escalate a dose reduced for toxicity.

Toxicity	Action
Grade 3 related organ / non-hematologic	Hold*; ↓ 1 dose level
Moderate or severe proteinuria	↓ 1 dose level Consider temporary discontinuation of therapy in severe proteinuria*
Hypertension	Treat appropriately (refer to Management of Angiogenesis Inhibitor (AI)-Induced Hypertension). Reduce dose or hold as appropriate.

Grade 4 related organ/ non-hematologic; uncontrolled hypertension/crisis; RPLS; heart failure; wound dehiscence	Discontinue

*Do not start new cycle until toxicities have recovered to ≤ grade 2, platelets ≥ 100 x 10^9/L, and ANC ≥ 1.5 x 10^9/L.

Hepatic Impairment

Axitinib exposure is increased in moderate hepatic impairment, but has not been studied in patients with severe impairment.

Hepatic impairment	**Starting dose**
Mild hepatic impairment (Child-Pugh class A)	No dose adjustment required
Moderate hepatic impairment (Child-Pugh class B)	↓ dose by approximately 50%
Severe hepatic impairment (Child-Pugh class C)	Do not use (no data)

Renal Impairment

Creatinine Clearance (mL/min)	**Dose**
15 - 89	No dosage adjustments required.
< 15	Use with caution.

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F - Adverse Effects

Refer to axitinib drug monograph(s) for additional details of adverse effects

Most Common (≥50%)	Common (25-49%)	Less Common (10-24%)	Uncommon Side Effects (<10%), but may be Severe or Life-Threatening
• Increase in creatinine (may be severe) • Diarrhea	• Hypertension (may be severe) • Fatigue • Anorexia • Nausea, vomiting • Hoarseness • Hyperglycemia • ↑ Amylase / lipase (may be severe) • Hand-Foot Syndrome (may be severe)	• ↑ LFTs (may be severe) • Constipation • Hypothyroidism • Electrolyte abnormalities • Myelosuppression ± infection, bleeding (may be severe) • Cough/dyspnea • Mucositis • Musculoskeletal pain • Abdominal pain • Headache • Rash • Hypoglycemia • Dysgeusia • Proteinuria • Dyspepsia	• Venous thromboembolism • Arterial thromboembolism • Artery aneurysm / dissection • Cardiotoxicity • RPLS / PRES • GI perforation / fistula • Hyperthyroidism

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G - Interactions

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

- Avoid strong CYP3A4 inhibitors if possible due to ↑ axitinib exposure and/or toxicity. Axitinib dose reduction is recommended if co-administration with potent CYP3A4 inhibitors is necessary.
- Avoid strong CYP3A4 inducers and, if possible, moderate CYP3A4 inducers due to ↓ axitinib efficacy.
- Avoid administering drugs that increase gastric pH (e.g. antacids, PPIs, H2 antagonists) 2 hours before to 2 hours after axitinib.

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H - Drug Administration and Special Precautions

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

Administration:

- Tablets should be swallowed whole with a glass of water, with or without food.
- Grapefruit, starfruit, Seville oranges, their juices or products should be avoided during treatment.
- If a dose is missed, patient should skip the missed dose and take the next dose at the next scheduled time.
- Store at room temperature (25°C). Excursions permitted to 15-30°C.

Contraindications:

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

Other Warnings/Precautions:

- Use with caution in patients at risk of or who have a history of arterial or venous thromboembolism.
- Use with caution in patients at risk of bleeding. Axitinib is not recommended for use in patients with untreated brain metastases, a history of pulmonary embolism in the past 6 months or active bleeding in the past 3 months.
- Use axitinib with caution in bradycardic patients or patients at risk of bradyarrhythmia.

- Clinical trials excluded patients with uncontrolled hypertension at baseline or a recent history of MI, uncontrolled angina, coronary/peripheral artery bypass graft, symptomatic CHF, cerebrovascular accident, TIA, deep vein thrombosis or pulmonary embolism.
- Tablets contain lactose; carefully consider use in patients with hereditary galactose intolerance, severe lactase deficiency or glucose-galactose malabsorption.

Pregnancy/Lactation:

- This regimen should not be used 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 at each visit
- Blood pressure; Baseline and at each visit; start within a week after beginning treatment; more frequent after dose changes or interruptions
- Liver function tests (ALT, AST and bilirubin); Baseline and at each visit
- Renal function tests; Baseline and at each visit
- Thyroid function tests; Baseline and as clinically indicated
- Proteinuria; Baseline and as clinically indicated
- Signs and symptoms of cardiotoxicity; Baseline and periodically during treatment
- Clinical toxicity assessment for bleeding, thromboembolism, neurological and GI effects; At each visit

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

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J - Administrative Information

Outpatient prescription for home administration

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K - References

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

Rini BI et al. Comparative effectiveness of axitinib versus sorafenib in advanced renal cell carcinoma (AXIS): a randomised phase 3 trial. Lancet 2011;378:1931-9.

Rini BI et al. Phase II study of axitinib in sorafenib-refractory metastatic renal cell carcinoma. J Clin Oncol 2009;27(27):4462-8.

PEBC Advice Documents or Guidelines

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

April 2024 Updated Pregnancy and Lactation 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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